

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	7	homoallyl adj amine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L2	105294	ozone	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L3	302	homoallyl	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L4	33	L2 and L3	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L5	5	L2 same L3	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L6	2	("20030097005").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:19
L7	4	("2003097005").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:19
L8	7	("2200788").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:19
L9	23	"2200788"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L10	2	("6794542").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:19
L11	8	("9802410").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:19

EAST Search History

L12	0	("aminoadjacid").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:19
L13	341842	amino adj acid	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L14	5110	L2 and L13	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L15	299	L2 same L13	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L16	581729	beta	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L17	579380	amine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L18	21	L15 same L16	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L19	304137	acetic adj acid	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L20	267	L2 near5 L19	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L21	0	L3 same L20	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L22	0	L13 same L20	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L23	1514	L2 same L19	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19

EAST Search History

L24	394	L2 near10 L19	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L25	17	L20 same L17	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L26	5	"1351737"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L27	14	L20 near5 L17	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L28	0	L20 near1 L17	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L29	15	L20 near10 L17	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:23
L30	348	(560/40).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:30
L31	657	(546/335).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:32
L32	608	(562/553).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:32
L33	1599	I30 or I31 or I32	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:33
L34	0	I3 and I33	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:33

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NEWS 17 FEB 26 CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
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NEWS 20 MAR 20 MARPAT now updated daily
NEWS 21 MAR 22 LWPI reloaded
NEWS 22 MAR 30 RDISCLOSURE reloaded with enhancements
NEWS 23 APR 02 JICST-EPLUS removed from database clusters and STN
NEWS 24 APR 30 GENBANK reloaded and enhanced with Genome Project ID field
NEWS 25 APR 30 CHEMCATS enhanced with 1.2 million new records
NEWS 26 APR 30 CA/Caplus enhanced with 1870-1889 U.S. patent records
NEWS 27 APR 30 INPADOC replaced by INPADOCDB on STN
NEWS 28 MAY 01 New CAS web site launched
NEWS 29 MAY 08 CA/Caplus Indian patent publication number format defined
NEWS 30 MAY 14 RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS 31 MAY 21 BIOSIS reloaded and enhanced with archival data
NEWS 32 MAY 21 TOXCENTER enhanced with BIOSIS reload
NEWS 33 MAY 21 CA/Caplus enhanced with additional kind codes for German patents
NEWS 34 MAY 22 CA/Caplus enhanced with IPC reclassification in Japanese patents

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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FILE LAST UPDATED: 13 Jun 2007 (20070613/ED)

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=> homoallyl amine

945 HOMOALLYL

279198 AMINE

258623 AMINES

424834 AMINE

(AMINE OR AMINES)

L1 43 HOMOALLYL AMINE

(HOMOALLYL(W)AMINE)

=> ozon?

L2 107785 OZON?

=> l1 and l2

L3 0 L1 AND L2

=> amino acid

1121857 AMINO

44 AMINOS

1121875 AMINO

(AMINO OR AMINOS)

4385732 ACID
1577794 ACIDS
4884863 ACID
(ACID OR ACIDS)
L4 714963 AMINO ACID
(AMINO(W)ACID)

=> 12(1)14

L5 433 L2(L)L4

=> beta

1459085 BETA
1325 BETAS
L6 1459162 BETA
(BETA OR BETAS)

=> 15and 16

MISSING OPERATOR L5AND L6

The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> 15 and 16

L7 82 L5 AND L6

=>.d 17 72-82 ti

L7 ANSWER 72 OF 82 CAPLUS COPYRIGHT 2007 ACS on STN
TI Structure of gentianine

L7 ANSWER 73 OF 82 CAPLUS COPYRIGHT 2007 ACS on STN
TI Protein problems. VII. 5-Glutamal, 4-aspartal, and derived peptides

L7 ANSWER 74 OF 82 CAPLUS COPYRIGHT 2007 ACS on STN
TI Stereochemical structures of kainic acid and its isomers

L7 ANSWER 75 OF 82 CAPLUS COPYRIGHT 2007 ACS on STN
TI Condensation of phthalidylideneacetic acid with amino acids

L7 ANSWER 76 OF 82 CAPLUS COPYRIGHT 2007 ACS on STN
TI Oxazoles and oxazolones

L7 ANSWER 77 OF 82 CAPLUS COPYRIGHT 2007 ACS on STN
TI The preparation of aldehyde compounds

L7 ANSWER 78 OF 82 CAPLUS COPYRIGHT 2007 ACS on STN
TI β -Acetamido- β ,.beta
.-dicarbalkoxypropionaldehydes

L7 ANSWER 79 OF 82 CAPLUS COPYRIGHT 2007 ACS on STN
TI Unsaturated amino acids. II. Allylglycine, .beta
.-methallylglycine, and crotylglycine

L7 ANSWER 80 OF 82 CAPLUS COPYRIGHT 2007 ACS on STN
TI β -(Hydroxyphenyl)ethylamines and their transformations.
III. Synthesis of benzyliisoquinolines under physiological conditions

L7 ANSWER 81 OF 82 CAPLUS COPYRIGHT 2007 ACS on STN
TI Constitution of cytisine

L7 ANSWER 82 OF 82 CAPLUS COPYRIGHT 2007 ACS on STN
TI Action of ozone on hydrogenated and non-hydrogenated bases of the morphine
series

=> d 17 79 ti fbib abs

L7 ANSWER 79 OF 82 CAPLUS COPYRIGHT 2007 ACS on STN
TI Unsaturated amino acids. II. Allylglycine, .beta
.-methallylglycine, and crotylglycine
AN 1949:2517 CAPLUS
DN 43:2517
OREF 43:574a-e
TI Unsaturated amino acids. II. Allylglycine, .beta
.-methallylglycine; and crotylglycine
AU Goering, Harlan L.; Cristol, Stanley J.; Dittmer, Karl
SO Journal of the American Chemical Society (1948), 70, 3310-13
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA Unavailable
GI For diagram(s), see printed CA Issue.
AB cf. C.A. 42, 8262c. $\text{CH}_2\text{:CHCH}_2(\text{AcNH})\text{C}(\text{CO}_2\text{Et})_2$, refluxed 8 h. with concentrated
HCl, gives 26% $\text{MeCH.CH}_2\text{CH}(\text{NH}_2).\text{CO.O.HCl}$ (I) and 34% $\text{CH}_2\text{:CHCH}_2\text{CH}(\text{NH}_2)\text{CO}_2\text{H}$
(II), m. 255-8° (decomposition; m.ps. corrected) (Fillman and Albertson, C.A.
42, 2930f, gave 212-15°). II, refluxed 5.5 h. with concentrated HCl,
gives 28% I and 32% II. II in an equivalent of 0.1 N HCl, evaporated at room
temperature in an air stream, gives the HCl salt, m. 164-8° (decomposition).
Reduction of II gives $\text{PrCH}(\text{NH}_2)\text{CO}_2\text{H}$. The free lactone from I yields
3,6-diketo-2,5-bis(2-hydroxypropyl)piperazine (III), m. 173-4°
[Fischer and Leuchs, Ber. 35, 3787(1902) gave 223-5°].
 $\text{CH}_2\text{:CMeCH}_2(\text{AcNH})\text{C}(\text{CO}_2\text{Et})_2$, refluxed 8 h. with concentrated HCl, gives 93% of
the
 γ -Me derivative (IV) of I, m. 210-11°. $\text{CH}_2\text{:CMeCH}_2\text{CH}(\text{NH}_2)\text{CO}_2\text{H}$ in
1 equivalent N HCl gives IV. IV and 2 N NaOH give γ -hydroxyleucine.
 $\text{AcNHCH}(\text{CO}_2\text{Et})_2$ and $\text{MeCH:CHCH}_2\text{Cl}$ give 80% Et crotylacetamidomalonate (V),
m. 47-8°; reduction in EtOH over Raney Ni at room temperature/30 lb. gives
 $\text{Bu}(\text{AcNH})\text{C}(\text{CO}_2\text{Et})_2$, m. 41-2° (Albertson, C.A. 40, 2796.7, reported
it as an oil). Et crotylacetamidocyanoacetate (VI), m. 56.5°, 76%;
basic hydrolysis of VI gives 50% (V gives 30%) crotylglycine, decompose
about 260°; 2-Bz derivative, m. 139° (Karrer and Itschner, C.A.
29, 6210.6, gave 157°). The structure of the amino
acids was established by reduction to known compds. and by
ozonolysis.

=> acetic acid

244039 ACETIC
22 ACETICS
244048 ACETIC
(ACETIC OR ACETICS)
4385732 ACID
1577794 ACIDS
4884863 ACID
(ACID OR ACIDS)
L8 214408 ACETIC ACID
(ACETIC(W)ACID)

=> 17 and 18

L9 5 L7 AND L8

=> d 19 1-5 ti

L9 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Chemistry and structure of ganefromycin
L9 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Securinine and allosecurinine

L9 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Total synthesis of strychnine

L9 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Constitution of conessine. X. Oxidation of conessine and pyrolysis of oxidation products

L9 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Oxazoles and oxazolones

=> d 19 1-5 ti fbib abs

L9 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Chemistry and structure of ganefromycin
AN 1994:107570 CAPLUS
DN 120:107570
TI Chemistry and structure of ganefromycin
AU Carter, Guy T.; Phillipson, Douglas W.; West, Robert R.; Borders, Donald B.
CS Lederle Lab., Am. Cyanamid Co., Pearl River, NY, 10965, USA
SO Journal of Organic Chemistry (1993), 58(24), 6588-95
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA English
AB Ganefromycins are antibiotics produced by *Streptomyces lydicus* sp. *tanzanius* having com. potential as performance enhancement agents for livestock. Ganefromycins are related to the elfamycin family of antibiotics but contain several unique chemical features which are the source of novel and unexpected chemical Reactions under mildly basic conditions resulted in the interconversion of α - and β -ganefromycin by a 1,2-acyl migration. Strong base causes elimination of a trisaccharide whose structure was solved by single crystal x-ray diffraction anal. of the triacetate of the reduced ring-opened triol. Ammonolysis yields the same rearranged product from either α - and β -ganefromycin. Evidence is provided for the mechanism of this rearrangement involving elimination of the saccharide to form a transient α , β -unsatd. carbonyl, Michael addition of ammonia, and intramol. transacylation. Ozonolysis and acidic methanolysis were employed to obtain simplified compds. for structure determination Ganefromycin β fragments in warm acetic acid solution, releasing the long-chain amino acid. ¹³C NMR data with assignments are provided for the degradation products.

L9 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Securinine and allosecurinine
AN 1963:403684 CAPLUS
DN 59:3684
OREF 59:687f-h,688a-e
TI Securinine and allosecurinine
AU Satoda, I.; Murayama, M.; Tsuji, J.; Yoshii, E.
CS Nippon Shinyaku Co., Kyoto, Japan
SO Tetrahedron Letters (1962) 1199-1206
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA Unavailable
GI For diagram(s), see printed CA Issue.
AB The previously isolated securinine (I), C₁₃H₁₅NO₂ m. 141-2°, [α]_D²⁵ -1089° (alkaline), pK_a 7.17, was isolated from Japanese *Securinea suffruticosa* and a structure proposed on the basis of phys. and chemical data. IR absorption bands at 1792, 1764 cm.⁻¹ (CCl₄) and a broad UV spectral band at 256 m μ (ϵ 18,200) indicated the presence of an

α , β ; γ , δ -unsatd. γ -lactone, recovered on acidification after alkaline hydrolysis. I hydrogenated by Pd-SrCO₃ in C₆H₆ or reduced with NaBH₄ in alc. gave a dihydro derivative, an α , β -unsatd. γ -lactone (II), C₁₃H₁₇NO₂, m. 53.5°, [α]_{27D} 5.9°, ν 1810, 1767 cm.⁻¹ (CCl₄), λ 215 m μ (ϵ 17,700), pKa' 8.35. I hydrogenated in alc. with Pd-C or prerduced PtO₂ gave a tetrahydro derivative, the γ -lactone (III), C₁₃H₁₉NO₂, m. 67-9°, pKa' 9.03, ν 1789 cm.⁻¹ (CCl₄), λ 210 m μ (ϵ 1760), λ 210 m μ (ϵ 140, HCl), indicating satn of III and the tetracyclic nature of I. II reduced with LiAlH₄ gave an oily diol (IV), C₁₃H₂₁NO₂; HCl salt m. 165°, ν 3226 cm.⁻¹ (KBr). The salt in AcOH ozonized gave HOCH₂CHO and an oily α -ketol (V), C₁₁H₁₇NO₂; HCl salt m. 213°, ν 3300, 1728 cm.⁻¹ (Nujol). V reduced Tollens reagent but did not react with Cu(OAc)₂ in hot AcOH or with CrO₃ in AcOH at 20°. V oxidized with HIO₄ gave an unidentified oxo-amino acid and gave a monoxime, m. 207-8°, under forced conditions. V hydrolyzed with tert-BuOK gave II indicating the impossibility of migration of the exocyclic double bond to an enol lactone. The tertiary nature of the OH group in V was indicated. I showed no NH absorption band in the IR and gave a MeI salt without change of the UV absorption maximum at 256 m μ , indicating that the N in I is isolated but near to the conjugated double bonds. The conjugated double bond system was supported by the NMR spectrum (60 Mc. in CHCl₃, Me₄Si as internal reference). I treated with Zn in alc. H₂SO₄ at 20° gave a lactam (VI), C₁₃H₁₅NO, m. 74-5°, [α]_{25D} 13.9° (alc.), ν 1634 cm.⁻¹ (KBr), λ 265, 272 m μ (ϵ 450,420), oxidized exhaustively with KMnO₄ to give o-HO₂CC₆H₄CO₂H. The smooth aromatization of I to VI was rationalized by a 2-step mechanism. VI oxidized with a limited amount of KMnO₄ gave a hydroxy lactam (VII), C₁₁H₁₃NO₂, m. 182-3°, ν 3300, 1661 cm.⁻¹, λ 253 m μ (ϵ 4460); hydrogenolyzed over Pd-C to a dehydroxy lactam (VIII), C₁₂H₁₃NO, m. 78-80°, ν 1675 cm.⁻¹, showing that the OH is benzylic. The possible structures of VI, VII, and VIII were discussed. I. MeI aromatized by Zn in H₂SO₄ gave an oily ester (IX), C₁₆H₂₃NO₂; HClO₄ salt m. 171-2°, ν 1724, 759 cm.⁻¹ (KBr), λ 266, 272 m μ (ϵ 840, 739). Treatment with Zn in AcOH gave an α , β -unsatd. γ -lactone; HClO₄ salt m. 197-9°, λ 215 m μ (ϵ 13,600), ν 1742, 1678 cm.⁻¹ I hydrogenated with Pd-C or prerduced PtO₂ and the product chromatographed over Al₂O₃, eluted with (Me₂CH)₂O to give III, and further eluted with C₆H₆ containing 2% MeOH gave a crystalline hexahydro derivative

(X),

C₁₃H₂₁NO₂, m. 223 5°, ν 3279, 1603- cm. (KBr), [α]_{24.5546} 47.6°. The hydroxy lactam treated with HClMeOH gave a γ -lactone, reconverted into X by percolation through Al₂O₃. In addition to I, it was possible to isolate another minor alkaloid, allosecurinine (XI), C₁₃H₁₅NO₂, m. 136-8°, [α]_{26D} -1082° (alc.), ν 1818, 1754, 1631 cm.⁻¹ (Nujol), λ 257 m μ (ϵ 15,400), pKa' 6.91; oxalate m. 174-6°. XI reduced with NaBH₄ gave a dihydroallosecurinine (XII), m. 85-6°, [α]_{26D} 25.2° (CHCl₃), ν 1818, 1739 cm.⁻¹, λ 215 m μ (ϵ 19,500). XI hydrogenated in alc. over prerduced PtO₂ and the product chromatographed over Al₂O₃ gave, in addition to XII, a hexahydro derivative, C₁₃H₂₁NO₂, m. 263°, [α]_{24.5D} 44.7° (CHCl₃), ν 3311, 1613 cm.⁻¹ No tetrahydro derivative was obtained under any hydrogenation conditions. XI aromatized with Zn in alc. H₂SO₄ gave a lactam, m. 69°, [α]_{24.5D} -32.7° (alc.), with an IR spectrum identical with that of VI. Oxidation of the lactam with KMnO₄ gave VII and it was therefore concluded that XI is a stereoisomer of I, possibly differing at the B/C ring juncture.

AN 1963:81712 CAPLUS
 DN 58:81712
 OREF 58:14022g-h,14023a-h,14024a-h,14025a-h,14026a-h,14027a-h,14028a-c
 TI Total synthesis of strychnine
 AU Woodward, R. B.; Cava, M. P.; Ollis, W. D.; Hunger, A.; Daeniker, H. U.;
 Schenker, K.
 CS Harvard Univ.
 SO Tetrahedron (1963), 19, 247-88
 CODEN: TETRAB; ISSN: 0040-4020
 DT Journal
 LA Unavailable
 OS CASREACT 58:81712
 GI For diagram(s), see printed CA Issue.
 AB cf. CA 49,9001h. For the synthesis of strychnine (I) the selected point
 of departure was 2-veratrylindole (II). Acetoveratrone (25 g.) and 16 ml.
 PhNHNH₂ swirled with 110 g. polyphosphoric acid with warming on a steam
 bath (exothermic reaction controlled by cooling) and the mixture heated 10
 min. on a steam bath, poured into ice-H₂O and extracted into 250 ml. hot
 CHCl₃, the organic layer washed with 100 ml. H₂O and the dried extract
 concentrated,
 the CHCl₃ replaced by MeOH and the crystalline product (54.4%, m.
 185-9°) recrystd. twice from CH₂Cl₂-MeOH gave II, m. 190-2°.
 PhNH₂ (50 ml.) heated (oil bath) with 15 g. ω-bromoacetoveratrone
 and the mixture refluxed 1 hr. (oil bath, 175°), cooled to 50°
 and poured into 500 ml. ice-H₂O containing 50 ml. dilute HCl, the H₂O-washed
 precipitate taken up in CHCl₃ and the dried solution filtered through 50 g.
 Al₂O₃,
 the filtrate evaporated and the residue crystallized from EtOH-MeOH yielded
 39.5%
 II. The 1st steps in the construction of ring V involved transformation
 of II into 2-veratryltryptamine (III). II (5.6 g.) in 35 ml. 6:1
 dioxane-AcOH added to 6.3 g. 25% aqueous HNMe₂ and 1.71 g. 37% aqueous HCHO in
 15
 ml. cold AcOH and the mixture kept 2 hrs. at 20°, diluted with 300 ml.
 H₂O and the clear, filtered solution basified with ice-cold aqueous KOH, the
 precipitate
 washed thoroughly with H₂O and dried 12 hrs. in vacuo at 60°
 yielded 92% 2-veratrylgramine, m. 122-4°; picrate, m. 182-3°
 (Me₂CO-EtOH). The gramine (6.3 g.) taken up in 25 ml. boiling C₆H₆ and
 the filtered solution kept 2 hrs. at 0° with 20 g. MeI in 50 ml. C₆H₆,
 the precipitate washed with Et₂O, and then refluxed gently (N atmospheric)
 with stirring
 in 70 ml. HCONMe₂ containing 1.22 g. NaCN 1 hr. with evolution of NMe₃, the
 clear, cooled, yellow solution poured into 350 ml. ice-H₂O and the H₂O-washed
 precipitate dried at 60° in vacuo yielded 97% 2-veratryl-3-
 cyanomethylindole, m. 237-8° (alc.). LiAlH₄ (50 g.) in 1100 ml.
 absolute tetrahydrofuran (THF) stirred vigorously 1 hr. with 12 addns. of 10
 g. cyano compound at 5 min. intervals, the mixture stirred under reflux 2
 hrs., and the cooled suspension treated cautiously with 100 ml. saturated
 aqueous
 Na₂SO₄ followed by 1000 ml. CHCl₃ and anhydrous Na₂SO₄, the mixture filtered
 through Celite and evaporated in vacuo, the viscous residue triturated with
 500 ml. Et₂O and the light yellow crystals (104 g., m. 142-5°)
 twice recrystd. gave III, m. 146-8°; HCl salt, m. 270-80°
 (decomposition). Construction of rings V, III, and IV followed. OHCCO₂Et
 (33.6 g., freshly prepared from the corresponding ethyhemiacetal) in 250 ml.
 C₆H₆ added portionwise (exothermic reaction) to 97 g. III in 500 ml. warm
 C₆H₆, the solution refluxed 5 hrs. under a Dean-Stark head with separation of 5
 ml. H₂O and kept 16 hrs. at 5°, swirled with 500 ml. Et₂O, and the
 product isolated yielded 113.9 g. Schiff base (IV), m. 170-80°
 (C₆H₆), λ 224, 245, 308 mμ (ε 31,600, 16,400, 20,800,
 all detns. in alc.). IV (45 g.) and 45 g. p-MeC₆H₄SO₂Cl in 225 ml. C₅H₅N
 kept 18 hrs. at 20° and diluted with 300 ml. H₂O, the mixture cooled

(ice-H₂O) 30 min. and the H₂O and MeOH-washed product dried at 60° in vacuo gave 40.9 g. crystals, m. 143-5° recrystd. to give the indolenine (V), m. 145-6°, λ 234, 339 m μ (ϵ 23,600, 15,600). To set the stage for more considerable operations, two simple changes were effected. V (6 g.) in 70 ml. hot alc. slowly treated with 2.5 g. NaBH₄ in 2.5 ml. H₂O and 20 ml. alc. and the mixture heated gently 1 hr., the clear solution diluted with H₂O to incipient crystallization, and cooled to 5° yielded 5.11 g. crystals, m. 172-8°, recrystd. from CHCl₃-MeOH to give the corresponding indoline (VI), m. 180-1°, λ 233, 287, 300 m μ (ϵ 24,200, 4500, 3200); N-acetyl derivative (VII) m. 206° (CHCl₃MeOH), λ 235, 256, 280 m μ (ϵ 26,800, 18,000, 8000). VII (1.16 g.) in 25 ml. AcOH containing 10 drops of H₂O ozonized 22 min. with ozonized O containing 0.295 millimoles O₃/min. and the mixture poured into H₂O, the precipitate taken up in CHCl₃ and the solution washed with aqueous K₂CO₃. evaporated, and the neutral residue crystallized from MeOH yielded 29% of the muconic ester (VIII), m. 165° (184°), ultra-violet spectrum showing increasing absorption below 310 m μ with weak, ill-defined shoulder at 285 m μ and shallow maximum at 230 m μ (ϵ 24,100). VIII (800 mg.) refluxed 10 hrs. in 30 ml. 5% HCl in MeOH and the solution evaporated, the crystalline residue taken up in 22 ml. 10:1 MeOH-CHCl₃ and concentrated to 10 ml., kept several hrs. at 5° and the crystalline product (510 mg., m. 181-2°) recrystd. from MeOH yielded the pyridone (IX), m. 187-8° (MeOH), showing a highly characteristic ultraviolet and infrared absorption. Treatment of the total crude neutral product (15.95 g.) from ozonolysis of VII gave an over-all yield of 30% IX. IX (250 mg.) refluxed (N atmospheric) in 4 ml. MeOH containing 25 mg. Na and the solution cooled gave 41% 3-carbomethoxy-6H-pyrido[3,2,1-jk]carbazole-6-one, m. 180-1°, giving a strikingly characteristic ultraviolet absorption. The changes leading to the collapse of ring V were discussed; the difficulty caused by the p-MeC₆H₄SO₂ group was eliminated. IX (750 mg.) refluxed 3.5 hrs. with 250 mg. red P in 10 ml. 1:1 AcOH-47% aqueous HI and the filtered solution evaporated, the residue recovered repeatedly from AcOH and triturated with 5 ml. Me₂CO, the HI salt (400 mg.) acetylated 1 hr. at 20° in 3.2 ml. C₅H₅N and 4 ml. Ac₂O and the mixture kept 30 min. with 2 ml. H₂O, evaporated in vacuo and the semicryst. material rinsed with Et₂O, taken up in 8 ml. hot H₂O, and treated with 8 drops concentrated HCl, cooled and the N-acetylpyridone diacid (308 mg., m. 275°) taken up in 20 ml. MeOH, treated with freshly prepared CH₂N₂ in Et₂O to cessation of N evolution, kept 1 hr. at 5°, and excess CH₂N₂ destroyed with AcOH, the residue on evaporation taken up in EtOAc and diluted with Et₂O and C₆H₁₂ yielded 84% colorless N-acetylpyridone di-Me ester (X), m. 181.0-2.5° (EtOAc-Et₂O), exhibiting a typical N-phenylpyridone chromophore in the ultraviolet absorption spectrum. X (900 mg.) refluxed (N atmospheric) 20 min. in 20 ml. MeOH containing 1 g. Na and kept cold 16 hrs. yielded 87.5% Na salt (XI), taken up (100 mg.) in H₂O and acidified with HCl, extracted with CHCl₃ and the dried extract evaporated gave 80 mg. free enol ester (XII), readily soluble in aqueous NaHCO₃ to give a bright yellow solution, showing a pos., blue FeCl₃ reaction, and exhibiting an ultraviolet absorption spectrum differing markedly from those of the simple N-phenylpyridones. C₅H₅N (23 ml.) containing 3.7 g. p-MeC₆H₄SO₂Cl kept 10 hrs. at 20° with 768 mg. XI and diluted with 10 ml. H₂O, followed shortly by 80 ml. 5N HCl, extracted with CHCl₃ and the residue on evaporation of the neutral, washed solution crystallized from Me₂CO yielded

95% of the enol tolylsulfonate (XIII), m. 217° (Me₂CO), λ 234,312, 317, 350-80 mμ (ε 23,900, 13,800, 13,700, 3800). MeOH containing PhCH₂SNa (12 ml., prepared from 122 mg. Na and 670 mg. PhCH₂SH in

100

ml. absolute MeOH) heated with 230 mg. XIII and the clear solution kept at 20° (N atmospheric) 3 hrs., filtered, and the precipitate washed with cold MeOH gave the benzylthio ester (XIV), m. 256-7° (CHCl₃-MeOH) λ 207, 253, 312 mμ (ε 31,000, 13,000, 14,000). XIV (500 mg.) in 100 ml. alc. refluxed 3 hrs. with 3 ml. alc. Raney Ni slurry and filtered, the residue washed with 100, 50, 50, and 50 ml. hot alc., and the residue on evaporation (398 mg.) taken up in a min. of Me₂CO, diluted with Et₂O, and filtered yielded 84% unsatd. ester, recrystd. twice from Me₂CO-Et₂O to give a colorless sample, m. 234°, λ 232, 310, 365 mμ (ε 25,600, 12,100, 4150). The unsatd. ester (252 mg., m. 185-215°) in 75 ml. alc. hydrogenated 2 min. at 20° with 50 mg. 10% Pd-C and the filtered solution evaporated yielded 72.5% racemic cis Me ester (XV), m. 186° (Me₂CO-Et₂O), softening at 160° exhibiting a typical N-phenylpyridone chromophore. The mother liquors yielded, on long standing, a small amount (20 mg.) of highly crystalline trans ester, m. 212° (Me₂CO-Et₂O). XV (440 mg.) refluxed 1 hr. in 15 ml. 2:1 MeOH-H₂O containing 220 mg. KOH and the MeOH evaporated in vacuo, the residue diluted with H₂O, and the nonacidic material (16 mg.) extracted with CHCl₃, the alkaline layer acidified with dilute H₂SO₄, and extracted with CHCl₃ yielded

388 mg.

acidic material, recrystd. from MeOH to yield 59% rhombs, m. 271° (rapid heating), recrystd. 3 times from CHCl₃-MeOH to give racemic trans acid (XVI), m. 284° (decomposition, slow heating), showing an infrared spectrum identical with the spectra of the corresponding synthetic resolved acid and the acid from the degradation of I. A further crop of 48 mg. XVI was obtained by methylation of the mother liquors with CH₂N₂ and hydrolysis. XVI (30 mg.) in MeOH treated with excess CH₂N₂ in Et₂O and the residue on evaporation recrystd. twice from Me₂CO gave 24 mg. trans Me ester (XVII), m. 212° (Me₂CO-Et₂O), infrared spectrum identical with the spectra of the corresponding synthetic resolved ester and the ester from the degradation of I. XVII was identical in every respect with the Me ester, m. 212°, isolated as a byproduct from hydrogenation of the unsatd. ester. XVI (249 mg.) heated gently with quinidine [231 mg., m. 263-4° (CHCl₃-MeOH)] in 4 ml. 1:1 CHCl₃-MeOH and the residue on evaporation crystallized from CHCl₃-Me₂CO gave 114 mg. quinidine

salt

dihydrate, m. 160-72°, taken up in 10 ml. 1:1 H₂O-10% aqueous K₂CO₃ and extracted with CHCl₃, the aqueous solution acidified and extracted with CHCl₃

to give 51

mg. 1-trans-N-acetyl acid (XVIII), m. 295-300° (CHCl₃-MeOH), identical with the acid obtained by degradation of I. The apparently simple task of forming ring VI actually presented considerable preliminary difficulty since the trans disposition of Nb and the CO₂H group in XVIII required prior inversion at C-14. XVIII (200 mg.) refluxed 1 hr. in 20 ml. 1:1 C₅H₅N-Ac₂O and the residue on evaporation taken up in 20 ml. CHCl₃, the solution shaken 5 min. with 10 ml. cold 10% aqueous K₂CO₃ and the CHCl₃

solution

washed with 10 ml. H₂O, the dried solution evaporated and the residue chromatographed from 2.5 ml. C₆H₆ on 8 g. neutral Al₂O₃, the column eluted with C₆H₆ and the eluate (235 mg.) treated with CH₂Cl₂-Et₂O yielded 93 mg. product, recrystd. to give 27.5% enol acetate (XIX), m. 250-5°, recrystd. from MeOH-Et₂O to give an anal. sample, m. 260-3°, λ 240, 258,335, 347,362 mμ (ε 21,300, 13,200, 7100, 8400, 5800). XIX (130 mg.) refluxed vigorously 6 hrs. in 6 ml. 1:1:1 concentrated HCl-AcOH-H₂O and the residue on evaporation taken up in dilute

H₂SO₄, made

alkaline with concentrated NH₄OH, and extracted with CHCl₃ gave 100 mg.

colorless oily

Me ketone (XX), showing a typical N-phenylpyridone chromophore ultraviolet

absorption spectrum. XX (100 mg.) kept 15 hrs. at 20° with 72.5 mg. SeO₂ in 6 ml. absolute alc. and the mixture refluxed 1 hr. on a steam bath, treated with C and the filtered solution evaporated, the residue taken up in 10 ml. 1:1 C₆H₆-CHCl₃ and filtered through C, diluted with 10 ml. CHCl₃ and extracted twice with 5 ml. dilute H₂SO₄, washed successively with 10 ml. H₂O,

10

ml. aqueous KHCO₃, and 5 ml. H₂O, the solvents evaporated and the neutral green oil (50 mg., containing traces of Se) taken up in 5 ml. MeOH, shaken with deactivated Raney Ni and the filtered solution diluted to 25 ml. with H₂O, heated 5 min. on a steam bath and treated with C, filtered while still hot and the residue washed twice with 5 ml. boiling H₂O, the cooled filtrate extracted with CHCl₃ and the residue on evaporation (21 mg.) crystallized from

MeOH gave

12.4% dehydrostrychninone methanolate (XXI), m. 172-4° (resolidifying and m. 254-8°), $[\alpha]_{24D} -521 \pm 4^\circ$ (c 1.05, CHCl₃), identical with material prepared by degradation of I. The facile enolization of XX was confirmed by reversion to the enol acetate XIX, by formation of the methylthio derivative (XXII), and by the production of the degraded ketone (XXIII) by hydrolysis of XIX with NaOH-MeOH in the presence of atmospheric O. XX (100 mg.) refluxed (N atmospheric) 4 hrs. in 10

ml. 1:1

Ac₂O-C₅H₅N and the residue on evaporation taken up in CHCl₃, the residue on evaporation (143 mg.) chromatographed on 5 g. neutral Al₂O₃ and eluted with 40 ml. 3:1 C₆H₆-CHCl₃ gave 99 mg. yellow foam, crystallized from CH₂Cl₂-Et₂O to yield 16.6% XIX, m. 260-3°. XIX (100 mg.) heated 30 min. in an open vessel on a steam bath with 1 ml. 2N aqueous NaOH in 5 ml. MeOH and the solution diluted with 20 ml. H₂O, the MeOH evaporated in vacuo at 40° and the aqueous solution extracted successively with 20, 10, and 10 ml. CHCl₃, the combined extract evaporated and the semisolid residue (57 mg.) crystallized

from MeOH

yielded 28 mg. material, m. 234-6°, recrystd. twice from MeOH-Et₂O to give XXIII, m. 237°, λ 237, 294, 319, 332, 347 m μ (ϵ 17,800, 13,200, 9200, 10,300, 7200). XX (2.18 g.), 1.60 g. p-MeC₆H₄SO₂SMe, and 3.6 g. anhydrous KOAc refluxed (N atmospheric) 4 hrs. in

AcOH

and the solvent removed at 60° in vacuo, the dark green residue taken up in CHCl₃ and the solution washed twice with aqueous 2N Na₂CO₃,

extracted 5

times with 10 ml. 2N H₂SO₄, the acid extract basified with NaOH and extracted with CHCl₃, the ketone (1.94 g.) isolated as HCl salt monohydrate and recrystd. from MeOH gave 1.236 g. colorless needles of XXII.HCl.H₂O, m. 187-8° (MeOH). XXII.HCl.H₂O (543 mg.) shaken 1 hr. with 15 ml. 2:1 C₅H₅N:Ac₂O and the solution kept 10 hrs. at 20°, the solvents evaporated in vacuo and the residual oil taken up in 25 ml. CHCl₃, washed successively with 10 ml. each dilute H₂SO₄, dilute NaOH, and H₂O, and the dried extract

evaporated

gave 476 mg. colorless foam, crystallized from C₆H₆-C₆H₁₂ to give 393 mg. product, m. 221-3°, recrystd. from MeOH to yield the N-Ac derivative, m. 223°, giving a typical N-phenylpyridone chromophore ultraviolet absorption spectrum. The conversion of dehydrostrychninone to I was undertaken. Purified C₂H₂ passed as a gentle stream into 30 ml. liquid NH₃ and stirred magnetically with portionwise addition of 150 mg. Na with change of color of the mixture from deep blue to gray, the NH₃ evaporated and the mixture heated 30 min. at 70° the dry HC.tplbond.CNa stirred in 20 ml. freshly prepared absolute THF and stirred at 0° with addition of dehydrostrychninone (XXI, 220 mg., heated 30 min. at 180-90° in a high vacuum with change of color to bright yellow on loss of MeOH) in 10 ml. THF, the mixture stirred 1 hr. at 20° and diluted with 25 ml. CHCl₃ and 10 ml. N HCl, the washed (aqueous KHCO₃, H₂O) and dried organic layer

evaporated

and the yellow foam (172 mg.) diluted with MeOH yielded 53% carbinol, recrystd. 3 times from CHCl₃-MeOH to give the ethynyl carbinol (XXIV), m. 302-5°. XXIV (500 mg.) in 50 ml. MeOH hydrogenated 3 min. with

deactivated Lindlar catalyst with uptake of 35.3 ml. H and the filtered solution evaporated in vacuo gave 432 mg. vinyl carbinol, m. 244-5° (MeOH). LiAlH₄ (200 mg.) in 40 ml. Et₂O refluxed with magnetic stirring in a Soxhlet apparatus and each half-filled thimble treated with 1 ml. solution (260 mg. XXIV in 10 ml. 1:1 Et₂O-THF), the completed addition mixture refluxed 1 hr. and diluted with 40 ml. CHCl₃ at 0°, decomposed with 2 ml. MeOH and 6 ml. H₂O, the organic layer separated and the hydroxide slurry washed 3 times with 20 ml. CHCl₃, the combined CHCl₃ exts. shaken with 30 ml. H₂O and the dried extract evaporated, the green oily residue (257 mg.) taken up in

10

ml. CHCl₃ and extracted 3 times with 10 ml. N H₂SO₄, the aqueous layer basified with NH₄OH and extracted with CHCl₃, the basic product (243 mg.) chromatographed on 7.5 g. neutral Al₂O₃ and eluted with 40 ml. 1:1 C₆H₆-CHCl₃ gave 156 mg. carbinol (XXV), crystallized from HCl in MeOH to yield 30% crystals, m. 192-200°, recrystd. from MeOH containing a drop of H₂O to give the hydrochloride dihydrate, C₂₁H₂₂N₂O₂·HCl·2H₂O, m. 195-205° (decomposition). The HCl salt (195 mg.) heated 2.5 hrs. at 120° (oil bath) in a 10-cm. long, sealed, glass tube in 4 ml. 30% HBrAcOH and 20 mg. red P with 3 cm. immersion to permit reflux, the cooled mixture filtered, and the residue on evaporation refluxed 30 min. with 10 ml. N H₂SO₄, diluted with 10 ml. H₂O and the mixture boiled 1 hr., the clear yellow solution clarified with 200 mg. C and filtered while still hot, the cooled filtrate extracted twice with CHCl₃ and the aqueous layer basified with 3 ml. NH₄OH, extracted 4 times with CHCl₃ and the residue on evaporation

chromatographed

on 4 g. activated neutral Al₂O₃ and eluted with 4:1 and 1:1 C₆H₆-CHCl₃, CHCl₃, and 20:1 CHCl₃-MeOH gave a combination of 72.5 mg. partially crystalline and crystalline (m. 202-9°) fractions, recrystd. from MeOH to give 18.5 mg. material, m. 206-11°, recrystd. 3 times to yield synthetic isostrychnine (XXVI), m. 229-30° (evacuated capillary tube), [α]_D²⁵ 23 ± 4° (c 2.54, alc.), identical with natural material prepared according to Leuchs and Schulte (CA 37, 34397). The noncryst. material from the combined fractions and the XXVI mother liquors evaporated in vacuo and the residue (84 mg.) acetylated at 20° in 5 ml. Ac₂O and 0.5 ml. C₅H₅N, the acetylated product (98 mg.) chromatographed on 3 g. neutral Al₂O₃ and eluted with 5:3 C₆H₆-CHCl₃ gave 65 mg. oily XXVI acetate, λ 5.86μ. XXVI (7mg.) and the acetate (65mg.) kept 15 min. in a long, sealed, glass tube at 20° with 4 ml. 1.5% alc. KOH and the mixture heated 5 hrs. on a steam bath, the fluorescent mixture diluted with 20 ml. CHCl₃ and washed twice with H₂O, the residue on evaporation (70 mg.) chromatographed on 4 g. neutral Al₂O₃ and eluted with 4:1 C₆H₆-CHCl₃, the crystalline product (9.5 mg.) taken up in 1 ml. dilute H₂SO₄ and freed from 1.5 mg. nonbasic material with CHCl₃, the aqueous layer made alkaline with

NH₄OH

and extracted with CHCl₃, the extract evaporated and the colorless product (8 mg.)

recrystd. 3 times from CHCl₃-Et₂O gave brilliant colorless cubes of I, m. 275-85°, identical with natural material by m.p. and infrared spectral detns. Following completion of the total synthesis of I, miscellaneous reactions starting from dehydrostrychninone were reported.

XXI (1.016 g.) heated 2 hrs. to 200° in vacuo and the yellow ketone taken up in 100 ml. dry C₆H₆, 3 g. activated Zn, 0.5 ml. freshly distilled BrCH₂CO₂Me, and traces of iodine and HgCl₂ added, and the mixture refluxed with vigorous stirring (N atmospheric), the mixture treated 5 times at 40 min. intervals with 2 g. Zn and twice at 90 min. intervals with 0.5 ml.

BrCH₂CO₂Me, the mixture refluxed altogether 5 hrs. and the cooled mixture diluted with 20 ml. MeOH, the clear solution decanted at 0° into 100 ml. 2N AcOH and the residual Zn washed twice with 50 ml. CHCl₃, the organic layer extracted with 100 ml. dilute aqueous NH₄OH and 50 ml. H₂O, and the aqueous

layer washed

with 30 ml. CHCl₃, the combined CHCl₃ evaporated and the red-yellow oil (1.365 g.) taken up in 10 ml. Me₂CO and cooled to 0° gave 410 mg. crystals, recrystd. from Me₂CO to give the hydroxy ester A (XXVII), m.

260-4°, λ 5.78 μ . The mother liquor residues (1.1 g.) chromatographed on 50 g. neutral Al₂O₃ and eluted with 1:1 C₆H₆-CHCl₃ gave 540 mg. colorless oil, diluted with 5 ml. Me₂CO to give 209 mg. XXVII (total yield 42.5%). The Me₂CO solution concentrated and the product (70 mg.)

recrystd. 4

times from C₆H₆-Et₂O gave the stereoisomeric hydroxyester B (XXVIII), m. 242-4°, λ 5.83 μ . XXVII (115 mg.) refluxed 5 hrs. in 15 ml. Ac₂O and the residue on evaporation chromatographed on 5 g. Al₂O₃, eluted with 1:1 C₆H₆-CHCl₃, and the pale, yellow, oily product crystallized from C₆H₆-C₆HCl₂ gave 101 mg. acetoxy ester, m. 198-203°, λ 5.77, 5.79 μ (poorly resolved doublet). The acetoxy ester (59 mg.) pyrolyzed 12 hrs. at 200-50° in a high vacuum and the colorless sublimate recrystd. from MeOH gave 45 mg. α , β -unsatd. ester (XXIX), m. 244-8°, λ 5.82 μ . XXIX (42 mg.) in 10 ml. alc. hydrogenated with 10 mg. Pd-C with adsorption of 1 mole equivalent H and the filtered solution evaporated, the oily product chromatographed on 2 g. neutral Al₂O₃ and eluted with 1:1 C₆H₆-CHCl₃ gave 43 mg. material, recrystd. from MeOH to yield 38 mg. colorless saturated ester (XXX), m. 265-8° (CHCl₃-MeOH), λ 5.78, 5.98, 6.17, 6.27 μ (typical triplet N-phenylpyridone absorption). Reduction of XXIX or XXX with LiAlH₄ in Et₂O or THF gave very complex mixts. of products from which no pure compds. were isolated. A series of model redns. were recorded in connection with the reduction of the aromatic α -pyridone ring in XXI to the Δ 12-dihydro- α -pyridone oxidation level, by addition of H at C-8 on the concave, more hindered side of the mol. Reduction of XXI by LiAlH₄ in boiling Et₂O gave the base in which the pyridone had been reduced precisely to the desired dehydro level. The structure was verified through the observation that the corresponding acetate (XXXI) was further reduced by LiAlH₄ to a new base (XXXII), also produced by similar reduction of strychninone b acetate (XXXIII; cf. CA 14, 1328). A proposed mechanism of reduction received confirmation from the interesting observation that strychninolone a acetate (XXXIV; cf. CA 8, 2718) is reduced under similar conditions. The base (300 mg., from XXXIV) in 15 ml. THF added slowly with stirring to 300 mg. LiAlH₄ in 15 ml. THF and the mixture refluxed 4 hrs., cooled to 10° and diluted with 30 ml. CHCl₃, swirled with 5 ml. H₂O and decanted, the slurry washed with CHCl₃ and the combined CHCl₃ extracted 3 times with 10 ml. dilute H₂SO₄, the acid exts. made alkaline with

NH₄OH

and extracted with CHCl₃ gave 275 mg. basic reduction product, directly acetylated

at 20° with 3.3 ml. 10:1 Ac₂O-C₅H₅N and the basic acetate (235 mg.) chromatographed on 7 g. neutral Al₂O₃, eluted with C₆H₆, and the yellow material crystallized from MeOH-Et₂O gave 102 mg. product, m. 190-3°, recrystd. from Me₂CO-C₆H₁₂ to give dihydrostrychninol (XXXV) acetate, m. 193-4°, λ 254, 283, 292 μ (ϵ 15,000, 4500, 3800), λ 6.00, 6.23, 5.79 μ . XXXIII (300 mg.) similarly reduced with LiAlH₄ to a basic product (237 mg.) and crystal. from alc. gave the imino alc. XXXII, m. 240-3° (decomposition), λ 6.20, 6.74 μ , but no band in the 6 μ region. The mother liquors acetylated with 3.3 ml. 10:1 Ac₂O-C₅H₅N followed by chromatographic purification on neutral Al₂O₃ gave 144 mg. imino acetate, m. 208-10° (MeOH-Et₂O), λ 6.20, 6.75, 5.79 μ . XXI (190 mg.) in the thimble of a Soxhlet extracted into a boiling suspension of 200 mg. LiAlH₄ in 30 ml. absolute Et₂O 24 hrs. and the isolated basic material (156 mg.) chromatographed from CHCl₃ on 4 g. activated neutral Al₂O₃, the eluate (106 mg.) acetylated and the crystalline acetate (97 mg., m. 215-18°) recrystd. from MeOH-Et₂O gave strychninol b acetate XXXI, m. 217-19°, λ 254, 284, 294 μ (ϵ 12,100, 4200, 3800), λ 6.0, 6.24, 6.75, 5.79 μ , also produced by reduction of dehydrostrychninolone (or its acetate) with LiAlH₄. XXXI (63 mg.) extracted into a boiling suspension of 60 mg. LiAlH₄ in 20 ml. absolute Et₂O 4 hrs. and the isolated basic material (59 mg., m. 215-30°) recrystd. from MeOH gave 44 mg. pure XXXII, m. 237-40° (decomposition); acetate m. 206-9°. It was confirmed

that the racemic synthetic acid and its ester were identical with the corresponding optically active compds. obtained by degradation along essentially known lines but significantly modified with addition of new terminal stages. Oxidative degradation of I according to Leuchs and Schwaebel (CA 8, 694) yielded 23-4% strychninonic acid (XXXVI), m. 257-9°. XXXVI (44 g.) reduced with 245 g. 2.5% Na-Hg in 220 ml. at pH 7-8 (maintained by gradual addition of 2N HCl) and the clear solution made strongly alkaline with 80 ml. 10% aqueous NaOH gave 32 g. product, m. 208-13°, twice recrystd. from alc. to give strychninolone a, m. 228-31°. The ketone (20 g.) heated 2 hrs. on a steam bath in 110 ml. 10:1 Ac2O-C5H5N and the residue on evaporation taken up in 200 ml. CHCl3, washed successively with 20 ml. N HCl, 20 ml. saturated aqueous KHCO3, and 50 ml.

H2O, and filtered through anhydrous Na2SO4 and the residue on evaporation crystallized

from MeOH-Et2O yielded 88% product, m. 237-42°, twice recrystd.

from alc. to almost colorless crystalline XXXIV, m. 242-4°. XXXIV (19.8

g.) in 300 ml. Ac2O at 115° streamed through vigorously with dry

HCl and the solvent evaporated in vacuo, the residual oil taken up in 200 ml.

CHCl3 and the solution washed with 100 ml. aqueous KHCO3 and 100 ml. H2O, the dried solution evaporated, and the residue crystallized from alc. yielded 85%

XXXIII,

m. 214-18° (with loss of EtOH at 135°). XXXIII (9.3 g.) and

17 g. Hg(OAc)2 refluxed 2 hrs. in 900 ml. AcOH and the solution decanted at

60°, streamed through 45 min. with H2S and filtered twice through

Celite, the oily residue on evaporation taken up in 100 ml. CHCl3 and treated

with 200 mg. C, the clear, filtered solution washed with 10 ml. dilute H2SO4, 20

ml. aqueous NaHCO3, and 30 ml. H2O, the residue on evaporation treated with

C6H6-Et2O and the crystalline product (7.9 g., m. 268-78°) twice

recrystd. from MeOH gave dehydrostrychninolone acetate, m. 282-5°,

saponified (7 g.) with 800 ml. concd, aqueous NH4OH to yield 5.7 g.

dehydrostrychninolone (XXXVII), m. 228-30°. CrO3 (5.7 g.) added

cautiously to 50 ml. C5H5N (external cooling) and the red slurry treated

with 5.7 g. XXXVII in 50 ml. C5H5N, the mixture kept 16 hrs. at 20°

and poured into 500 ml. H2O, shaken vigorously with addition of 500 ml. CHCl3

and 3 g. Celite, filtered, and the aqueous layer extracted with CHCl3, the

CHCl3

layer washed with 200 ml. H2O and the combined dried CHCl3 solns. evaporated

in vacuo, the residue taken up in 100 ml. CHCl3 and washed with 40 ml.

0.5N H2SO4, 20 ml. 10% aqueous NaHCO3, and 40 ml. H2O, the residue on

evaporation

boiled in 125 ml. 4:1 C6H6-CHCl3 with C and Celite and the filtered solution

concentrated to 25 ml., diluted with MeOH and heated briefly, the solution

cooled and

the combined crops (2.45 g., 1.55 g.) recrystd. from MeOH gave

dehydrostrychninolone methanolate XXI, m. 175-80° (loss of MeOH),

solidifying to bright yellow crystals, m. 254-8°, infrared spectrum

identical with that of synthetic material. Pulverized XXI (250 mg.)

shaken 10-20 min. with 6.7 ml. aqueous 0.29N Ba(OH)2 and the clear yellow

solution treated dropwise with 1.40 ml. aqueous 2.10% H2O2 in 10 min., the

mixture

stirred 3 hrs. at 20° and treated with 1.75 ml. N H2SO4, the

stirring continued 15 min. and the solution filtered through Celite, the

clear yellow solution (pH 9) extracted 3 times with 10 ml. CHCl3, the aqueous

layer

concentrated in vacuo at 50° to 2 ml. and diluted with 3 ml. Me2CO, slowly

cooled and the product (115 mg., m. 300-5°) recrystd. from

MeOH-H2O-Me2CO gave the trans amino acid, m.

305-8° (decomposition). The acid (200 g.) kept 16 hrs. at 20°

with 5 ml. Ac2O and 2 ml. C5H5N and the residue on evaporation taken up in

CHCl3 and extracted with dilute H2SO4 yielded 52% trans-N-acetylamino acid, m.

295-300°, identical in all respects with the levorotatory XVIII.

The acid (9 mg.) and 10 mg. quinidine taken up in CHCl3 and the residue on

evaporation recrystd. twice from MeOH-Me₂CO gave 6 mg. colorless needles, m. 160-72°, undepressed on admixt. with the quinidine salt dihydrate isolated from XVIII. Esterification of the acid with CH₂N₂ in Et₂O gave the Me ester, m. 196°, [α]_D²² -292 ± 5° (c 1.14, CHCl₃), identical with XVII in the synthetic series. The acid (34 mg.) refluxed 4 hrs. in 2 ml. 5% HCl in MeOH and the residue on evaporation crystallized from MeOH-Et₂O, the HCl salt (23 mg., m. 245-50°) taken up in 1 ml. C₅H₅N and heated 30 min. on a steam bath with 35 mg. p-MeC₆H₄SO₂Cl, the mixture diluted with 0.3 ml. H₂O and evaporated in vacuo, the residue taken up in 30 ml. 1:2 CHCl₃-Et₂O and washed with 5 ml. dilute H₂SO₄, 5 ml. 10% aqueous KHCO₃, and 10 ml. H₂O, the dried CHCl₃-Et₂O solution evaporated and the residue (26 mg.) recryst. from MeOH-Et₂O gave 20 mg. trans-tolylsulfonylamino Me ester, m. 229°. Infrared measurements were used for control purposes through the investigation and 26 spectra, taken in CHCl₃, of pure substances in the main line of synthesis were recorded.

L9 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Constitution of conessine. X. Oxidation of conessine and pyrolysis of oxidation products
 AN 1958:50699 CAPLUS
 DN 52:50699
 OREF 52:9163f-i,9164a-i,9165a-i,9166a-g
 TI Constitution of conessine. X. Oxidation of conessine and pyrolysis of oxidation products
 AU Haworth, R. D.; Michael, M.
 CS Univ. Sheffield, UK
 SO Journal of the Chemical Society (1957) 4973-83
 CODEN: JCSOA9; ISSN: 0368-1769
 DT Journal
 LA Unavailable
 GI For diagram(s), see printed CA Issue.
 AB cf. C.A. 51, 3641g. Oxidation of conessine (I) and its derivs. gave evidence favoring proposed structures for "α-oxyconessine" (II) and dioxyconessine (III). Oxidation and pyrolytic expts. similar to those used in the degradation of steroids gave I derivs. with a ruptured B ring, 5-membered B ring, and A and B rings degraded to a basic fragment which may be approached by synthesis. The nomenclature of the derivs. was based on the trivial name "conanine" for structure A with arbitrary α-configuration at position 5, on which basis I and III became 3. beta.-dimethylamino-5-conanine and 5,6-dihydroxy-3.beta.-dimethylaminoconanine, resp. Steroid nomenclature rules were applied and seco and nor prefixes used to indicate reductive bond rupture and ring contraction, resp., leading to the designation 5-oxo-5,8-seco-B-bisnorconanine for the parent structure (B). The system employed by Pinder and Robinson (C.A. 47, 1109g) was used for the nomenclature of the tricyclic ring. For products with unassigned configurations ordinary bond lines were used. Oxidation of I with SeO₂ in hot H₂O according to Bertho, et al. (C.A. 42, 2609b) gave 3β-dimethylamino-5-hydroxy-6-conanine (IV), m. 158°, ν 3382 cm.⁻¹, acetylated according to Bertho (C.A. 45, 1608g) to the 5-AcO derivative (IVa), m. 128°, hydrolyzed with N KOH in MeOH to IV, stable to refluxing with Al(iso-PrO)₃ or Al(tert-BuO)₃ in PhMe-cyclohexanone. IV (250 mg.) in 20 ml. AcOH kept 87 hrs. with 90 mg. CrO₃ in 1.5 ml. H₂O and 4.5 ml. AcOH, the solution made alkaline with NaOH, extracted with Et₂O, and the gummy product (230 mg.) crystallized from petr. ether and Me₂CO gave an isomeric epoxide (V), C₂₄H₄₀N₂O₂, m. 163-4°. IV (100 mg.) and 0.15 ml. 30% H₂O₂ in 2.5 ml. 2N H₂SO₄ heated on a steam bath 3 hrs., the excess peroxide destroyed with SO₂, the solution basified, extracted 3 times with Et₂O, the extract evaporated, and the gummy peroxide (85 mg.) crystallized from Me₂CO gave 21 mg. crystalline peroxide (Va), m.

225-6°. The Me₂CO mother liquors evaporated, the residue taken up in ligroine, chromatographed on 2 g. Al₂O₃, eluted with 1:1 Et₂O-ligroine, and the oily product crystallized from dilute Me₂CO gave 28 mg. 3.β -dimethylamino-4,6-conadienine (VI), m. 116°, undepressed on admixt. with the product, m. 116°, of the action of POCl₃ on IV (cf. Bertho, C.A. 46, 6129e), λ 2320, 2390, 2470 Å. (log ε 4.3, 4.35, 4.2). Attempts to convert V and Va into triols were unsuccessful and oxidation of IV must be regarded as only provisional. I (500 mg.) in 10 ml. pure dioxane refluxed 3 hrs. with 780 mg. SeO₂, the solvent evaporated, the residue diluted with H₂O, the Se centrifuged off, the aqueous layer basified, extracted with Et₂O, and the gummy product (180 mg.) chromatographed in C₆H₆ on 5 g. Al₂O₃ and eluted with C₆H₆ and CHCl₃ gave 60 g. base, C₂₄H₄₀N₂O₂, m. 179-80° (C₆H₁₂) [picrate, m. 110° (Me₂CO)], and 27 mg. base, C₂₄H₃₈N₂O₂, m. 240° (C₆H₆-ligroine). Similar results were obtained in C₅H₅N and in MeOCH₂CH₂OH. IVa (1 g.) and 1 g. OsO₄ in 100 ml. dry Et₂O kept 16 days at 20°, evaporated, the residue shaken overnight with 5 g. mannitol and 20 ml. N KOH, the alkaline solution extracted 3 times with Et₂O, the combined exts. evaporated to 690 mg. residue, 303 mg. residue refluxed 1 hr. in 10 ml. N KOH in MeOH, evaporated, the residue taken up in H₂O, extracted with Et₂O, and the product chromatographed on 8 g. Al₂O₃ and eluted with Et₂O and Et₂O-CHCl₃ gave 82 mg. IV and 110 mg. base, C₂₄H₄₀N₂O₂, m. 239-41° (C₆H₁₂). The above residue (276 mg.) heated 2 hrs. on a steam bath with 10 ml. H₂SO₄, basified, extracted with Et₂O, and the product chromatographed on 8 g. Al₂O₃ gave 90 mg. VI and 38 mg. unidentified substance, m. 180° (C₆H₁₂). IVa (410 mg.) in 70 ml. Me₂CO shaken with 420 mg. KMnO₄ in 70 ml. Me₂CO, evaporated, the residue taken up in Et₂O, the solution washed with dilute aqueous NaOH, the dried extract evaporated, and the gum (337 mg.) chromatographed from Et₂O-ligroine over 9 g. Al₂O₃ and eluted gave 210 mg. IVa and an oily base, C₂₆H₄₀N₂O₃, m. 128° [MeI derivative, m. 234-5° (Me₂CO)], indicating that the basicity of 1 tertiary amino group had been destroyed either by oxidation of an N-Me to an N-CHO group, or by oxidation of an NCH₂ group to an NCO group. Evidence in favor of the structure of (III) (dioxyconessine) was obtained by CrO₃ oxidation of III, ν 3382, 3143 cm.⁻¹, prepared according to Bertho (C.A. 42, 2609b) rather than by Warnecke's method [Arch Pharm. 226, 248 (1888)]. III (200 mg.), 4 ml. C₅H₅N, and 1 ml. Ac₂O heated 2 hrs. on a steam bath, the mixture evaporated in vacuo, and the residue diluted with 1 ml. H₂O and kept 2 days over H₂SO₄ in vacuo gave 5,6-diacetoxy-3β -dimethylaminoconanine monoacetate (VII), m. 194-6° (decomposition) (Me₂CO), converted by taking up in dilute HCl, basifying with dilute NaOH, filtering, and crystallizing the washed precipitate from dilute MeOH to the diacetylated base hydrate (VIIa), m. 130-5° (after resinification); MeI derivative, m. 296° (decomposition) (Me₂CO). Attempted partial hydrolysis of VIIa was unsuccessful. III (565 mg.) in 40 ml. AcOH and 200 mg. CrO₃ in 2.5 ml. H₂O and 7.5 ml. AcOH kept 3 days at 20°, the excess CrO₃ destroyed with 5 ml. MeOH, the basified solution extracted continuously 12 hrs. with CHCl₃, and the extract evaporated gave 3β -dimethylamino-5-hydroxy-6-oxoconanine (VIII), m. 281-2° (alc.), subliming at 180°/10 mm., ν 3382, 1698 cm.⁻¹, converted by refluxing 5 days with 98-100% HCO₂H into an isomer, m. 193-5° (Me₂CO), and a substance, m. 204-5° (decomposition) (Me₂CO-ligroine). VIII gave no semicarbazone, Ac derivative, or enol acetate and was inert to SeO₂, (CH₂CO)₂NBr, BzH, KIO₄, and POCl₃. Oxidative fission of ring B of III was effected with hot CrO₃. III (11 g.) in 100 ml. 10% H₂SO₄ heated on a steam bath with slow addition of 5.5 g. CrO₃ in 200 cc. H₂O, the mixture kept 1 hr. at 100°, cooled, basified with Ba(OH)₂, centrifuged, the residue washed with warm H₂O, the combined washings and aqueous liquors boiled, the volatile bases passed into aqueous picric acid to give NHMe₂ picrate, m. 157-8° (alc.), the

nonvolatile aqueous solution saturated with CO₂, filtered from precipitated BaCO₃, the filtrate evaporated in vacuo, and the residue (8.8 g.) crystallized from Me₂CO containing a small amount of H₂O gave 5-oxo-5,6-seco-3-conenin-6-oic acid (IX) sesquihydrate, C₂₂H₃₃NO₃·1.5H₂O, m. 193-6° (decomposition), λ 2270 Å. (log ε 4.0), stable to heating 12 hrs. at 60°/0.01 mm. The insol. residue (6.5 g.) heated 6 hrs. with 150 ml. alc. HCl, and the gum (6.3 g.) chromatographed in ligroine on 120 g. Al₂O₃ and eluted with C₆H₆-ligroine and Et₂O yielded 3.3 g. Et 5-oxo-5,6-seco-3-conenin-6-oate (IXa), b_{0.03} 195°, λ 2270 Å. (log ε 4.0), and 120 mg. of an unidentified substance, m. 103-4° (ligroine). After rupture of ring B appropriate conditions for the addnl. removal of ring A following the elegant methods of Cornforth, et al. (C.A. 47, 11278i), were studied. IX (6.2 g.), 15 g. dry K₂CO₃, and 6 g. Fe filings heated with a free flame, the yellow distillate from 2 runs mixed with the Et₂O extract of the nonvolatile material, and the basic material extracted by washing the Et₂O extract with dilute HCl (leaving 380 mg. nonbasic material in the Et₂O), recovered by basification, isolated with Et₂O, chromatographed in C₆H₆-ligroine on 125 g. Al₂O₃, and eluted with C₆H₆-ligroine and C₆H₆ gave 2.20 g. oil, B-nor-3,5-conadiene (X), λ 2400, 2450 Å. (log ε 4.1, 4.1), unreactive with maleic anhydride, and 190 mg. ketone (XI), m. 98-9° (dilute Me₂CO), sublimed at 80°/0.01 mm., ν 3436, 1738 cm.⁻¹, giving a pos. Liebermann test [semicarbazone, m. 162-3° (dilute Me₂CO)]. A provisional structure, arising from the undetected aminotricarboxylic acid intermediate, was suggested for the ketonic base XI. X (196 mg.) in 10 ml. alc. hydrogenated at 20° with 390 mg. 5% Pd-C in 12 hrs. gave 180 mg. oily dihydro compound with no characteristic ultraviolet absorption maximum; MeI derivative, m. 257-8° (Me₂CO-Et₂O). III with hot CrO₃ and the amino acid mixture (15 g.) (containing IX) in 100 ml. alc. shaken 15 hrs. in H in the presence of 4 g. 10% Pd-C, filtered, and the solvent evaporated gave 5-oxo-5,6-secoconanin-6-oic acid (XII), no characteristic ultraviolet absorption spectrum in alc. XII (6.6 g.) and 3.3 g. dry K₂CO₃ heated, the residue distilled in vacuo, the distillate from 2 runs combined, and the basic fraction (6.2 g.) isolated as above, chromatographed in ligroine on 180 g. Al₂O₃, and eluted with ligroine and ligroine-Et₂O gave 3.37 g. colorless oil and 1.65 g. pale yellow oil. Crystallization of the former from Me₂CO gave B-nor-5-conenine (XIII), m. 78-9° and the Me₂CO mother liquors gradually deposited a dimorphous prismatic form, m. 78-9°. Inoculation of the latter oil with this form caused rapid solidification and in subsequent reactions the dimorphous forms were undistinguishable. XIII liberated iodine from HIO₃ but had no characteristic ultraviolet absorption spectrum; HCl salt, m. 268° (decomposition) (MeOH-Me₂CO); picrate, m. 100° (dilute Me₂CO); MeI derivative, m. 261-2° (Me₂CO-C₆H₆); dihydro derivative (prepared in AcOH with prerduced PtO₂), m. 67-8° (Me₂CO), not liberating iodine from HIO₃. XIII in Et₂O treated with 2N HCl, the crystalline HCl salt kept overnight in vacuo, the gummy product warmed 40 min. in dilute HCl on a steam bath, and the dried crystalline product recrystd. from Me₂CO-MeOH gave the isomeric HCl salt, m. 274° (decomposition), converted to the isomeric base B-nor-8(9)-conenine (XIIIa), m. 114.5-15°, stable to reduction with prerduced PtO₂ in AcOH, but readily liberating iodine from HIO₃. The behavior of XIII toward a number of oxidizing agents was examined HIO₃, H₂O₂ in acid solution, and

CrO₃ gave intractable gums, and ozonolysis, followed by catalytic reduction of the ozonide, gave nonbasic amorphous material. Pyrolysis of the crude ozonolysis product resulted in the formation of 2-methy cyclohexanone and a noninvestigated higher-boiling nonbasic material unstable to light. XIII (128 mg.) and 1 g. KIO₄ in 40 ml. N H₂SO₄ kept 20 hrs. at 20°, cooled to 0°, basified with NaOH, and extracted with Et₂O gave 38 mg. 4,5,6-trihydroxy-B-norconanin, m. 234-5° (decomposition) (MeOH-Me₂CO). The mother liquors evaporated and the residue solidified under ligroine at 0° yielded 35

mg. 5,6-transdihydroxy-B-norconanine (XIV), m. 168-9 (C₆H₁₂). XIII (1 g.) and 1 g. OsO₄ in 80 ml. Et₂O refluxed 5 days, the precipitated osmic ester washed with Et₂O, the filtrate and washings evaporated to give 333 mg. XIII, the precipitate shaken 12 hrs. with 5 g. mannitol in 30 ml. N KOH, the mixture diluted with 52 ml. H₂O, extracted 4 times with CHCl₃, the H₂O-washed extract evaporated, the gum (650 mg.) chromatographed in Et₂O on 20 g. Al₂O₃, eluted with Et₂O, and the gummy product (450 mg.) triturated with ligroine gave 265 mg. 5,6-cis-dihydroxy-B-norconanine (XIVa), m. 184-5° (C₆H₁₂). XIVa (100 mg.) and 100 mg. KIO₄ in 5 ml. N H₂SO₄ kept 40 hrs. at 20°, cooled to 0°, and basified with dilute NaOH gave 95 mg. 4,8-hydroxymethylene-5-oxo-5,8-seco-B-bisnorconanine (XV), m. 179-80° (C₆H₁₂), ν 1700, 3345 cm.⁻¹; semicarbazone, m. 220-1° (Me₂CO). In an attempt to induce a reversed aldolization the aldol base was treated with alkali. XV (50 mg.) in MeOH heated 90 min. (N atmospheric) with 160 mg. KOH in 1 ml. H₂O, and the solution diluted with 5 ml. H₂O, neutralized to pH 7 with 2N H₂SO₄, and filtered gave 29 mg. 5-hydroxy-5,6-seco-B-norconanin-6-oic 5,6-lactone, m. 131-2° (ligroine). XV (328 mg.) and 164 mg. K₂CO₃, pyrolyzed and the product treated as above, gave 42 mg. 2-methylcyclohexanone and 109 mg. basic fractions, purified by chromatography in ligroine over Al₂O₃ to 16 mg. unidentified oil; picrate, m. 226° (decomposition) (Me₂CO). XV (100 mg.) and 31 mg. CrO₃ in 9.5 ml. AcOH and 0.5 ml. H₂O kept 50 hrs. at 20°, the excess CrO₃ destroyed by addition of 5 ml. warm alc., the AcOH evaporated in vacuo, the residue basified with dilute NaOH solution, extracted with Et₂O, and the product crystallized from dilute Me₂CO gave 4,8-carbonyl-6-oxo-5,8-seco-B-bisnorconanine (XVI), m. 121-2°. XVI (100 mg.), 5 ml. saturated Ba(OH)₂ solution, and 5 ml. H₂O heated 2 hrs. on a steam bath, the mixture freed from unchanged XVI (3 mg.) with Et₂O, the aqueous layer saturated with CO₂, the mixture filtered, the filtrate evaporated, and the crude 5-oxo-5,6-seco-B-norconanin-6-oic acid (XVII) esterified with CH₂N₂ in Et₂O gave the Me ester (XVIIa), m. 131-2° (ligroine); MeI derivative, m. 290° (decomposition) (Me₂CO). XIVa (100 mg.) in 1 ml. 10% H₂SO₄ warmed 30 min. on a steam bath with 40 mg. CrO₃ in 2 ml. H₂O and the amino acid fraction isolated as above gave 52 mg. gum, methylated in Et₂O with CH₂N₂ to XVIIa. XVIIa (50 mg.) heated at 335-40° in an evacuated sealed tube, and the product chromatographed in ligroine on 1 g. Al₂O₃ and eluted with Et₂O-ligroine gave 25 mg. oily 5-hydroxy-5,6-seco-B-norcon-4-enin-6-oic 5,6-lactone; MeI derivative, m. 299-300° (decomposition) (MeOHMe₂CO). XVII (200 mg.) and 100 mg. dry K₂CO₃ distilled over a free flame, the distillates from 4 runs separated into 160 mg. nonbasic (2-methylcyclohexanone) and 380 mg. basic fractions, and the basic material taken up in ligroine, filtered from 120 mg. insol. material, chromatographed over 9 g. Al₂O₃, and eluted with ligroine and ligroine-Et₂O gave 50 mg. colorless oil and 132 mg. pale yellow oil with a powerful odor. The picrate of the colorless oil recrystd. 3 times from alc. gave 18 mg. de-AB-8-conenine picrate, m. 178-9° (decomposition); this treated with LiOH and the free base reduced with prerduced PtO₂ in AcOH gave de-AB-conanine; picrate, m. 153-4° (dilute Me₂CO). The picrate of the yellow oil twice recrystd. from Me₂CO-CCl₄ gave 9 mg. de-N-methyl-de-AB-8-conenine picrate, m. 236-8 (decomposition), decomposed with LiOH, and the de-N-methylde-AB-8-conenine extracted into Et₂O. It had a very powerful odor and gave a pos. Liebermann nitroso test.

DN 49:15976

OREF 49:3137a-i,3138a-i,3139a-i,3140a-i,3141a-i,3142a-i,3143a-i,3144a-i,3145a-i,3146a-i,3147a-i,3148a-i,3149a-i,3150a-i,3151a-b

TI Oxazoles and oxazolones

AU Cornforth, J. W.; Clarke, H. T.; et al.

CS Oxford Univ.; Princeton Univ. Press

SO Chemistry of Penicillin (1949) 688-848

DT Journal

LA Unavailable

GI For diagram(s), see printed CA Issue.

AB OXAZOLE SECTION: New methods for constructing the oxazole ring have been devised and the behavior of functional groups elucidated. The synthesis of oxazoles and imidazoles from K β -hydroxy- α -(α -alkoxyalkylideneamino)acrylates is given. A mixture of 51.1 g. AmCN and 24.5 g. EtOH was kept with 19.2 g. dry HCl below 0° for 2 wk, decomposed with 74 g. K₂CO₃ in Et₂O and distilled. The crude AmC(OEt):NH (62.4 g.), b₁₁ 52-65°, was shaken with cold aqueous H₂NCH₂CO₂Et.HCl for 1 h. The upper layer was fractionated to yield Et α -ethoxycaprylideneaminoacetate (I), b_{0.5} 91°, saponified on gentle warming to AmCO₂Et. The corresponding Me α -methoxycaprylideneaminoacetate (Ia), b_{0.1} 74°, was similarly prepared. A solution of 0.85 g. K in 2.5 g. EtOH and 14 g. Et₂O was diluted to 50 mL. with Et₂O, cooled to -15° and treated with a similarly cooled mixture of 4.85 g. I and 3.2 g. HCO₂Et, yielding after 3 h. at -10°, 2.6 g. of hygroscopic needles of C₅H₁₁C(OEt):NC(CO₂Et):CHOK (II). The corresponding K Me β -hydroxy- α -(α -methoxycaprylideneamino)acrylate (IIa) was obtained in 3.2 g.-yield from 3.75 g. Ia. Treatment of 2.6 g. II and 1.25 g. DL-penicillamine in 5 cc. EtOH with alc.-HCl gave crystalline DL-N-caproylpenicillamine, m. 137-8°. Treatment of II with ethereal HCl produced Et 2-amyl-oxazole-4-carboxylate, b_{0.07} 99° (dinitrophenyl-hydrazone, m. 165-6°; amide, m. 152°) saponified to 2-amyl-oxazole-4-carboxylic acid, m. 92-3° (PhNH₂ salt, m. 98.5-9.5°) readily decarboxylated to 2-amyl-oxazole, b. 172-3°; picrate, m. 84.5-5.5°. This general synthesis of 2-substituted oxazoles and their 4-carboxylic acids has been extended to Et 2-phenyloxazole-4-carboxylate, m. 69-70°, the corresponding acid, m. 209°, and carried through to the known 2-phenyloxazole. The method can be also applied to the synthesis of imidazoles. Treatment of I with aqueous NH₄OH gave 2-amylimidazole-4-carboxylic acid, m. 230° (decomposition); with MeNH₂.HCl or alc. H₂NCH₂CO₂Et.HCl, I produced, resp., Et 2-amyl-1-methylimidazole-4-carboxylate (III), m. 42-3°, and Et 2-amylimidazole-4-carboxylate-1-acetate (IIIa), m. 61°. Similarly, Ia gave Me 2-amyl-1-methylimidazole, m. 66.7°, and Me 2-amylimidazole-4-carboxylate-1-acetate, m. 107°. Hydrolysis of III and IIIa yielded 1-methyl-2-amylimidazole-4-carboxylic acid, m. 121-3°, and 2-amyl-4-carboxyimidazole-1-acetic acid, m. 132-4°. Starting from PhCH₂CN, Et 2-benzylimidazole-4-carboxylate-1-acetate, m. 111-2°, was likewise prepared, converted by treating with MeOH into a Me Et ester. On heating with aqueous NH₄OH and with PhNH₂, 2-amyl-oxazole-4-carboxylic acid was converted into 2-amylimidazole, m. 33-4° and 1-phenyl-2-amylimidazole, m. 143-4°. Synthesis of oxazoles by rearrangement of oxazolones. The Na salt of 2-benzyl-4-hydroxymethylene-5-oxazolone (2.7 g.) in 50 mL. absolute MeOH was treated with 5 mL. absolute Et₂O containing 0.38

g. HCl. The gummy product (2.28 g.) was taken up in 10 mL. absolute MeOH and heated for 30 min. with 6.2 mL. H₂O containing 0.42 g. NaOH. The residue on evaporation was dissolved in 10 mL. of iced H₂O, acidified with dilute HCl to

pH

6.5 and extracted with Et₂O, yielding 700 mg. 2-benzyl-oxazole-4-carboxylic acid, m. 158°. On heating at 220°, crude 2-phenyl-4-(α -hydroxyethylidene)-5-oxazolone rearranged to

2-phenyl-5-methyloxazole (IV), m. 184-5° (decomposition). Similarly, on heating to 230°, Na 4-hydroxymethylene-g-amyl-5-oxazolone rearranged to 2-amyl-oxazole-4-carboxylic acid. Evaporation of 2-(1-pentenyl)-4-(hydroxymethylene)-5-oxazolone in NaOH and fusion of the residue at 250° under reduced pressure yielded 2-pentenyl-oxazole-4-carboxylic acid, m. 145-7°. Incidental syntheses of oxazole derivs. The action of PhSO₃Ag on Me thiobenzylpenaldate di-Et acetal produced colorless prisms of 2-benzylloxazole-4-carboxylic acid, m. 156-7° and the dehydration of Et α-benzylamino-acetoacetate gave Et 2-phenyl-5-methyloxazole-4-carboxylate, m. 51-2°, hydrolyzed to the acid, m. 180-1°, decarboxylated at 220° in the presence of a trace of CuO to IV. Thus a reaction known to succeed with α-acylamino ketones and carboxylic esters is extended to . beta.-keto esters. The 2-substituted oxazoles and their 4-carboxylic acids and esters are feebly basic, readily oxidized by cold aqueous KMnO₄ but stable to Br in CCl₄. The ring opens on warming with 2,4-(O₂N)₂-C₆H₃NHNH₂ in 2N HCl with a tendency to formation of glyoxal osazone derivs. Rosenmund reduction of 2-amyl-oxazole-4-carboxylic acid chloride produced 2-amyl-oxazole-4-carboxaldehyde, b₈ 108° (2,4-dinitrophenylhydrazone, m. 172-3°), converted by warming with D-penicillamine-HCl in AcOH to the thiazolidine, devoid of antibiotic properties. From the corresponding Et ester, 2-benzyl-4-carboxyoxazole hydrazide, m. 81-3° and benzylamide, m. 121-2° were prepared. In attempts to synthesize the thiazolidine-oxazolone structure for penicillin, attention was directed to the preparation of 5-alkoxyoxazoles and many variations of the general method of dehydrating α-acylamino esters with P₂O₅ were introduced. By the use of PCl₅, P₂O₅, POCl₃, SOCl₂, and PhSO₂Cl, the following new oxazoles were prepared (substituent given): 2-Ph, 5-MeO, b₉ 141°; 2-Ph, 5-PhCH₂O, m. 56°; 2-PhCH₂, 5-EtO, b₁₅ 152-4°; 2-PhCH₂, 5-MeO, m. 31-2°; 2-Am, 5-EtO, b_{0.8} 82-5°; 2-Am, 5-MeO, b_{1.0} 60-65°; 2-(1-C₅H₉), 5-EtO, b₂₀ 125-8° (C₅H₉ = pentenyl); 2-(1-C₅H₉), 5-MeO, b₁₅ 108-10°; 2-PhCH:CH, 5-EtO, m. 35°; 2-PhCH:CH, 5-Ph CH₂O, picrate, m. 135° (decomposition); 2-Ph, 4-Me, 5-EtO, b₁₀ 151°; 2-Ph, 4-Me, 5-PhCH₂O, picrate, m. 112-13°; 2-PhCH₂, 4-Me, 5-EtO, b₁₅ 145-50°; 2-Am, 4-Me, 5-EtO, b₃ 92°; 2,4-Ph₂, 5-EtO, m. 47-8°; 2-Ph, 4-PhCH₂, 5-EtO, picrate, m. 105°; 2-Ph, 4-PhCH₂, 5-PhCH₂O, picrate, m. 117°; 2,4-(PhCH₂)₂, 5-EtO, b_{0.3} 145-50°; 2-Am, 4-PhCH:CH, 5-EtO, m. 92°; 2-Ph, 4-CO₂Et, 5-EtO, m. 75°; 2-Am, 4-CO₂Et, 5-EtO, b_{0.1} 122-5°; 2-(1-C₅H₉), 4-CO₂Et, 5-EtO, b_{0.2} 125°; 2-PhCH₂, 4-CO₂Et, 5-EtO, b_{0.1} 165°. The possibility of converting an alkoxyoxazole to the corresponding oxazolone was realized by the catalytic hydrogenation of 2 g. of 2-phenyl-5-benzylloxyoxazole in 30 mL. dry dioxane in the presence of Pd-black to 2-phenyl-5-oxazolone, m. 91°. The converse reaction, transformation of an oxazolone to an alkoxyoxazole, has also been achieved. Methylation of 3 g. of 2-phenyl-4-carbethoxy-5-oxazolone with 500 mg. CH₂N₂ in 50 mL. Et₂O yielded 2-phenyl-4-carbethoxy-5-methoxyoxazole, m. 72°. Similarly, methylation of 2-phenyl-4-carbomethoxy-2-oxazolin-5-one gave 2-phenyl-4-carbomethoxy-5-methoxyoxazole, m. 98°, identical with that prepared by the dehydration of BzNHCH(CO₂Me)₂ with PCl₅ in CCl₄. Attempts to obtain 5-alkoxyoxazole-4-carboxaldehydes covered a wide range. Formylation of BzNHCH₂CO₂Et and condensation with PhCH₂NH₂ in Et₂O gave Et .beta.-benzylamino-α-benzamidoacrylate, R'NHCH:C(CO₂Et)NHCOR (V; R = Ph, R' = PhCH₂), m. 108°, cyclized by PBr₃, POCl₃ or PCl₅ to 2-phenyl-4-benzylaminomethylene-5-oxazolone (VI), m. 134-7; Ac derivative, m. 140°. In the same way, Et β-benzylamino-α-phenylacetamido acrylate (VIa) with PBr₃ gave 2-benzyl-4-benzylaminomethylene-5-oxazolone (VIb). Dehydration of Et α-benzamido-β,β-diethoxypropionate with PCl₅-POCl₃ yielded 2-phenyl-4-(ethoxymethylene)5-oxazolone (VII). Distillation of benzyl α-benzamido-β,β-diethoxypropionate

.-diethoxypropionate gave a mixture of products including benzyl
 α -benzamido- β -ethoxyacrylate, m. 108-10°;
 benzyl 2-phenyloxazole-4-carboxylate, m. 106-7°; and VII. Attempts
 were made to cyclize α -benzyl- β -methyl-DL-
 phenylpenicilloate, $\text{HN} \cdot \text{CH}(\text{CO}_2\text{R}') \cdot \text{CMe}_2 \cdot \text{S} \cdot \text{CHCH}(\text{NHCOR})\text{CO}_2\text{CH}_2\text{Ph}$ (VIII, R = Ph,
 R' = Me) (VIIIa), m. 130°; dibenzyl-DL-phenylpenicilloate (VIII, R
 = Ph, R' = PhCH₂) (VIIIb), m. 107-8°; and DL-2-(carboxy-1-
 hexenoylaminoethyl)-5,5-dimethyl-4-carbometh-oxythiazolidine benzyl ester
 (VIII, R = 1-pentenyl, R' = Me). (VIIIc). The action of PCl₅ on VIII and
 VIIa gave definite evidence of formation of thiazolidinylalkoxyoxazoles
 and cyclization of VIIIb and chromatog. purification of the product gave benzyl
 2-(2-phenyl-5-benzoyloxy-4-oxazolyl)-5,5-dimethylthiazolidine-4-
 carboxylate, m. 120-5°, absorption band at 2850 Å. This reduced in
 EtOAc using a Pd-BaSO₄ catalyst with 2 mol H, corresponding to removal of
 2 PhCH₂ groups, yielded a product with no-antibiotic activity. The
 simpler thiazolidines were also investigated. The reaction of
 3-methyl-2-(benzamidocarbethoxymethyl)-thiazolidine with PCl₅ gave a
 Cl-containing product, converted by NaHCO₃ to a probable sulfoxide. With
 PCl₃, a product was obtained, which was converted by aqueous KOH to
 2-phenyl-4-hydroxymethylene-5-oxazolone. β -Methylaminoethyl
 mercaptan-HI (from 15 g. of 2-methylthiazoline-MeI) in 20 mL. H₂O was
 treated with 11 g. of crude Na salt of C,N-diformylglycine Et ester and
 neutralized with AcOH. After 15 h., NaHCO₃ was added and the dried CHCl₃
 exts. (120 mL.) were concentrated to give 6.55 g. of crude product, converted

by

treatment with 65.5 mL. of 10% HCl in EtOH to 4.4 g. of
 2-(aminocarbethoxymethyl)-3-methylthiazolidine-2HCl (IX), m.
 169-70° (decomposition). IX (10.0 g.) in 36.1 mL. of 2N NaOH and 35 mL.
 EtOH was stirred with 6.6 g. PhCH₂CS₂Me for 45 h., yielding 6.2 g. of
 colorless prisms of 2-[(phenylthioacetamido)carbethoxymethyl]-3-
 methylthiazolidine (X), m. 100-100.5°. Addition of 5.0 g X in 20 mL.
 CHCl₃ to 8.6 g. PhSO₃Ag and 2.5 mL. pyridine in 70-mL. CHCl₃ gave no
 identifiable organic products. The action of PhSO₃Ag on Me
 α -phenylthioacetamido- β ,.beta
 .-diethoxypropionate yielded a product from which Me-benzylpenaldate and
 2-benzoyloxazole-4-carboxylic acid were isolated. By the PCl₅ method it
 has been possible to prepare 4-(2-thiazolyl)-2-benzyl-5-ethoxyoxazole and
 2-(p-nitrophenyl)-4-(5,5-dimethyl-4-carbomethoxy-2-thiazolyl)-5-
 ethoxyoxazole. Attempts to introduce a CHO group into the 4-position of
 2-phenyl-5-ethoxyoxazole (XI) using PhNMeCHO and POCl₃ gave
 2-phenyl-4-anilinomethylene-5-oxazoline. With AcNHBr, XI gave
 2-phenyl-4-bromo-5-ethoxyoxazole, b0.8 128°. The oxidation of
 2-phenyl-4-methyl-5-ethoxyoxazole with SeO₂, CrO₃ or CrO₂Cl₂ resulted only
 in far-reaching breakdown. Condensation of PhCH₂CH₂COCO₂H with AcNH₂ or
 AmCONH₂ gave α -acetamido- and α -caproyl-amino- γ -
 phenylisocrotonic acid (XII). Treatment of the Et ester of XII with PCl₅
 afforded 2-amyl-4-styryl-5-ethoxyoxazole (XIII), disrupted by
 ozonization with production of BzOH and H₂NCOCO₂Et. XIII (5.7 g.) in
 100 mL. glacial AcOH was stirred with 9.0 g. of Pb(OAc)₄ for 3 h.,
 yielding 6.1 g. of 2-(1-acetoxyamyl)-4-styryl-5-ethoxyoxazole, m.
 90-1°, degraded by distillation with loss of AcOH to 2-(1-pentenyl)-4-
 styryl-5-ethoxyoxazole (XIV), m. 100°, reduced catalytically to
 XIII. Oxidation of 2.83 g. XIV in 30 mL. tert-BuOH containing 0.75 g. H₂O₂ and
 30 mg. OsO₄ at 40-50° for 2 h. produced PrCHO and
 5-ethoxy-4-styryl-oxazole-2-carboxaldehyde, m. 130.5°, converted
 into the thiazolidine, m. 169°, using DL-penicillamine.
 Cyclization of AmCONHCH(CO₂Et)₂ in dry alc. free CHCl₃ with PCl₅, yielded
 2-amyl-5-ethoxyoxazole-4-carboxylic acid (XIV), m. 63.4°, which on
 refluxing with PCl₅ in CHCl₃ gave Et 2-amyl-5-chlorooxazole-4-carboxylate
 (XV), b0.3 106°, catalytically reduced over Pd-BaSO₄ in xylene to
 2-amyl-oxazole-4-carboxylate, acidified to the free acid (XVa), m.
 93-4°, converted by alc. EtONa to XIV. Treatment of 2 g. XVa with
 1.09 g. PCl₅ in 10 mL. CHCl₃ and distillation produced the corresponding acid

chloride, b0.3 96°, converted by (NH₄)₂CO₃ in aqueous NH₄OH to the amide, m. 90°, which, distilled with P₂O₅, gave 2-amyl-5-chloro-4-cyanooxazole (XVb), b0.15 72°. Reduction of 3.0 g. XVb in a suspension of 5.7 g. anhydrous SnCl₂ in 40 mL. dry ether yielded unstable 2-amyl-5-chloro-oxazole-4-carboxaldehyde (XVI) (dinitrophenylhydrazones, m. 109-10°), rearranging in 3 days at room temperature or on low pressure distillation to 2-amyl-oxazole-4-carboxylic acid chloride. Despite its instability, XVI readily combined with D-penicillamine-HCl to produce D-2-(2-amyl-5-chloro-4-oxazolyl)-5,5-dimethylthiazolidine-4-carboxylic acid-HCl, m. 150-2° (decomposition). A similar series of compds. starting with Et 2-phenyl-5-ethoxyoxazole-4-carboxylate (XVII) and proceeding to the thiazolidine was later prepared. XVII was saponified to the crystalline acid (XVIIa), m. 148°, converted to the acid chloride (XVIIb), m. 105-6°, and to Et 2-phenyl-5-chlorooxazole-4-carboxylate, m. 68°, by refluxing in xylene for 1 h. The corresponding acid (XVIII), m. 178-4° (decomposition), was converted through the acid chloride, m. 118-20°, the amide, m. 183°, and the cyano compound, m. 112°, to 2-phenyl-5-chlorooxazole-4-carboxaldehyde (XIX), m. 91-3°. The addition of 1.14 g. aldehyde in 5 mL. EtOH and 10 mL. Et₂O to 0.93 g. D-penicillamine-HCl in 5 mL. H₂O and 0.65 g. AcONa, and passage of HCl through a filtered ethereal solution of the reaction product, yielded 1.5 g. of 2-(2-phenyl-5-chloro-4-oxazolyl)-5,5-di-methylthiazolidine-4-carboxylic acid-HCl, m. 178° (decomposition); Me ester-HCl, m. 120-2°; free acid, m. 166°; Me ester, m. 154°; PhCH₂ ester, m. 116-7°. The thiazolidine exhibited a low order of antibiotic activity. A similar series of 2-benzylloxazole derivs. have been prepared but the corresponding thiazolidine was inactive: 2-benzyl-5-ethoxy-oxazole-4-carboxylic acid, m. 118° (decomposition); Et ester, b0.1 165°; acid chloride, m. 81-2°; 2-benzyl-5-chlorooxazole-4-carboxylic acid, m. 183° (decomposition); Et ester, b0.02 170-5°; acid chloride, m. 156-7°; cyano compound, m. 49-50°; aldehyde [dinitrophenylhydrazones, m. 173°; semicarbazones, m. 185° (decomposition)]; 2-(2-benzyl-5-chloro-4-oxazolyl)-5,5-dimethylthiazolidine-4-carboxylic acid-HCl, m. 176-7° (decomposition). By refluxing 223 mg. XVIII in 3 mL. EtOH with 40 mg. Na, the Cl was replaced by the EtO group with formation of the corresponding acid, XVIIa. Distillation of the aldehyde XIX at 0.1 mm. gave 2-phenyloxazole-4-carboxylic acid chloride, m. 107-8°, transformed by stirring with cold concentrated aqueous NH₄OH to the amide. Similarly the

acid

chloride XVIIb was converted to the amide, m. 118-19°, rearranged by heating for a few min. at 140° to Et 2-phenyl-5-aminooxazole-4-carboxylate, m. 183deg;. All oxazoles found to undergo rearrangement may be formulated as 5-substituted oxazoles having a CO group in the 4-position, the general case being N:CR'.O.CR₃:CCOR₂ → N:CR'.O.CR₂:CCOR₃. Known examples of rearrangement are tabulated. Since the mol. is unstable when R₃ and R₂ are Et and Cl, resp., or when R₃ and R₂ are Cl and H, resp., it is deduced that the ethoxy aldehydes should show too great stability for successful synthesis. Cyclization of AmCONHCHCNCO₂Et with P₂O₅ in CHCl₃ gave 2-amyl-4-cyano-5-ethoxyoxazole, b0.03 98°, not reduced to the aldehyde by SnCl₂ in Et₂O. No 4-acetyloxazole was obtained from the MeMgI reaction product but the isolation of Et α-caproylaminoacetate (dinitrophenylhydrazones, m. 166-7°) indicated oxazole ring cleavage. The dehydration of 2-phenyl-5-ethoxyoxazole-4-carboxamide with POCl₃ or the ethylation with MeCHN₂ of the crude oxazolone obtained by treating BzNHCHCNCO₂H with Ac₂O produced 2-phenyl-4-cyano-5-ethoxyoxazole, m. 77°. The previously unknown 5-aminooxazoles were prepared thus: treatment of 7 g. BzNHCH(CN)CO₂Et, m. 138°, in 125 mL. CHCl₃ with 6.2 g. PCl₅ gave 4.5 g. Et 2-phenyl-5-aminooxazole-4-carboxylate, m. 185°, also prepared by the action of POCl₃ on Bz-NHCH(CONH₂)CO₂Et. Condensation of 1.18 g. H₂NCH-(CO₂Et)₂ with 1.13 g. PhNHOEt by heating for 30 min. at 110° gave the alternative compound, formulated as

2-phenyl-4-carbethoxy-5-imidazolone, m. 275°. Similarly were prepared Et 2-benzyl-5-aminooxazole-4-carboxylate (XX), m. 124° and the corresponding 2-benzyl-4-carbethoxy-5-imidazolone, m. 254° (decomposition); 2-(1-pentenyl)-4-carbethoxy-5-aminooxazole, m. 105°; 2-amyl-4-carbethoxy-5-aminooxazole (XXa), m. 104° and the corresponding 2-amyl-4-carbethoxy-5-imidazolone, m. 230° (decomposition). On heating at 170° for 5 min., XXa was entirely converted into AmCONHCH(CN)CO₂Et, m. 83°. Heating either XX or PhCH₂CONHCH(CN)CO₂Et at 160-70° for 15 min. produced an equilibrium mixture with the open chain ester predominating. This same mixture was formed by heating 2-benzyl-5-ethoxyoxazole-5-carboxylic amide, probably through initial rearrangement to the aminooxazole. Stirring 35 g. NCCH₂CO₂CH₂Ph in 40 mL. of chilled glacial AcOH with saturated aqueous NaNO₂ (16.5 g.)

yielded

29 g. NCC(NOH)CO₂CH₂Ph, m. 119°, reduced with Al-Hg to NCC(NH₂)CO₂CH₂Ph, m. 95°, and benzoylated to NCCH(NHBz)CO₂CH₂Ph, m. 130°, converted by heating at 160° for 5 min. to 2-phenyl-4-carbobenzyloxy-5-aminooxazole, m. 203°. The 4-carbethoxy-5-aminooxazoles are feebly basic substances whose HCl salts dissociate readily. XXa.HCl, on boiling with ethereal EtOH gave AmCONHCH(CONH₂)CO₂Et, m. 150-1°, along with NH₄Cl. Treatment of 1 g. XXa in 10 mL. dry Et₂O at -15° with NOCl gave a low yield of Et 2-amyl-oxazole-4-carboxylate, m. 92-3°. Formylation of 15 g. BzNHCH₂CN in 200 mL. HCO₂Et and 100 mL. benzene by addition of NaOEt (from 2.16 g. Na) in 100 mL. benzene produced, after treatment of the intermediate BzNHC(:CHONa)CO₂H with dilute H₂SO₄ to pH 4, 2-phenyl-5-aminooxazole-4-carboxaldehyde (XXI), m. 172-3°, probably in the tautomeric form. Formylation of AmCONHCH₂CN and distillation of the product yielded 2-amyl-oxazole-4-carboxylic acid amide, m. 154-5°, evidently by rearrangement of XXI. The action of POCl₃ on Bz-NHCH(CONH₂)₂ and AmCONHCH(CONH₂)₂, m. 231°, gave 2-phenyl-5-amino-4-cyanooxazole, m. 233° (Ac derivative, m. 202-3°), and 2-amyl-5-amino-4-cyanooxazole, m. 117°. These aminooxazoles could not be reduced to aldehydes.

Saturation of 0.52 g. PhCH₂CSNHCH(CN)CO₂Et, m. 157°, treated in 5 mL. dry EtOH with dry HCl at -10° and the solution evaporated after 12 h. at 20° in vacuo yielded 0.5 g. 2-benzyl-4-carbethoxy-5-aminothiazole, m. 180°. OXAZOLONE SECTION. Part. I. General Chemical of Oxazolones. Preparation of 2-Oxazolin-5-ones. The reaction of Ac₂O with α-acylamino acids is the most general procedure by which new oxazolones, O.CR:N.CR1R2.CO, have been prepared (substituents given): 2-Me, 4-iso-Pr, b10 60°; 2-PhCH₂, 4-Me, b0.5-1.0 122-3°; 2-PhCH₂, 4-iso-Pr, b0.5 115-17°; 2,4-(PhCH₂)₂, oil; 2-Am, 4-PhCH₂, b5 135-8°; 2-(2-pentenyl), 4-PhCH₂, b1.0 155-7°; 2-PhCH₂, 4,4-Me₂ (I), m. 59.5°; 2-Ph, 4-iso-Bu, m. 56-7°; 2-PhCH₂, 4-sec-Bu, b2.0 137-9°; 2-Ph, 4,4-C₅H₁₀, m. 71°; 2-PhCH₂, 4-Me, 4-PhCH:CH, m. 56-7°; 2-Ph, 4-CO₂Et, m. 147-8°; 2-Am, 4-CO₂Et, oil; 2-Ph, 4-(p-MeOC₆H₄CH₂); 2-PhCH₂, 4-(p-MeOC₆H₄CH₂); and 2-PhCH₂, 4-iso-Bu. Similarly, heating 100 g. BzNHCH₂CO₂H (II) in 300 mL. Ac₂O at 100° yielded 49 g. 2-phenyl-2-oxazolin-5-one (III), m. 94-5°, the only monosubstituted oxazolone prepared by this method.

By warming BzNHCHPhCH₂CO₂H in CHCl₃ with 1 equivalent of 2-benzyl-4-methyl-5-oxazolone, a good yield of 2-phenyl-4-benzyl-5-oxazolone, m. 68-9°, was obtained. Addition of 1 g. NaNO₂ in 20 mL. H₂O to 3 g. of BzNHC(CONHNH₂):-CHPh in 30 mL. N HCl gave α-benzamidocinnamic azide, m. 113-4° (decomposition), converted on boiling with EtOH or treatment with pyridine at room temperature to 2-phenyl-4-benzylidene-5-oxazolone (IV). Similarly, Me₂C:C(NHBz)-CON₃ was converted to 2-phenyl-4-isopropylidene-5-oxazolone (IVa). These type II (unsatd. substituent at the 4-position) unsatd. oxazolines are formed more readily than the above-listed type I (saturated substituent at the 4-position) saturated oxazolones to which the

azide

conversion could not be extended. Reduction of IV over Pd-C gave

2-phenyl-4-benzyl-5-oxazolone (V), m. 67-8°. IVa was similarly reduced in dioxane to give an oil which, treated with PhNH₂ in benzene, produced Me₂CHCH(NHBz)CONHPh, m. 211-2°. The possibility arose that any reagent capable of transforming an acid to its chloride might be expected to convert an α-acylamino acid to the corresponding oxazolone. Thus treatment of II in 15 mL. dioxane with 2 mL. PBr₃ gave III. Similarly, 14.5 g. PhCH₂CONHCHMe₂CO₂H in 150 mL. dioxane was treated with 18 g. PBr₃. The solid product suspended in dioxane and treated with slight excess of CH₂N₂ in ether yielded I, converted by PhCH₂NH₂ into PhCH₂CONHCHMe₂CONH₂, m. 122-3°. Treatment of PhCH₂CHNHBzCO₂H in pyridine with PBr₃ likewise gave the known V. Attempts to prepare 2-benzyl-5-oxazolone from PhCH₂CONHCH₂CO₂H gave an unstable oil, converted by PhCH₂NH₂ into PhCH₂CONHCH₂CONHCH₂Ph. Conversion of PhCH:C(NHBz)CO₂H into IV was effected by POCl₃, SOCl₂, pyridine, by ClCH₂COCl and K₂CO₃, and by AcCl in dioxane. Oxazolones have been produced by treating PhCH₂OCOC₂H with acylamino acids. Apart from direct dehydration, three methods are known for the preparation of type II oxazolones; the Erlenmeyer aldehydeacylglycine synthesis, the Bergmann-Stein reaction of N-(α-haloacyl) amino acids with Ac₂O, and the dehydration of β-hydroxy-α-acylamino acids. In that III reacts with Me₂CO in the presence of NaOAc to yield IVa in the absence of Ac₂O, it is suggested that III is an intermediate in the Erlenmeyer synthesis. In the presence of a little pyridine, BzH condenses with III to produce IV. Similarly, 2-phenyl-4-propylidene-5-oxazolone, m. 88-9°, was obtained in good yield from III and EtCHO. By adding Ac₂O dropwise with stirring to 17.9 g. II and 6.1 g. fused NaOAc in 580 mL. Me₂CO, refluxing for 3-4 h. at 59-62°, pouring the reaction mixture over 200 g. ice and diluting to 1500 mL. produced high yields (73%) of relatively pure 2-phenyl-4-isopropylidene-5-oxazolone, m. 98°. Condensation of II with (EtO)₂CHCHO and Ac₂O gave 4,4'-glyoxalidenebis(2-phenyl-5-oxazolone), m. 325° (decomposition). Though no acyl interchange in the Erlenmeyer synthesis occurs with II, the formation of 2-methyl-4-benzylidene-5-oxazolone occurs when either PhCH₂CONHCH₂CO₂H or AmCONHCH₂CO₂H (VI) is refluxed with BzH in the presence of Ac₂O and NaOAc. Refluxing VI (15.1 g.) with 13.1 g. AmCO₂Na and 61 g. (AmCO)₂O in 49 mL. Me₂CO for 24 h. at 75° gave α-caproyl-amino-β .,β -dimethylacrylic acid, m. 162-3°, converted by melting and heating in vacuo at 180-90° into 2-amyl-4-isopropylidene-5-oxazolone, b.p. 60-2°. By Bergmann's method, 2-methyl-4-isopropylidene-5-oxazolone (VII) and 2-methyl-4-sec-butylidene-5-oxazolone were prepared from Me₂CHCH₂CH(NHCOCH₂Cl)CO₂H and EtMeCHCH(NHCOCH₂Cl)CO₂H. Carter's method was used to prepare VII by the action of Ac₂O on Me₂C(OMe)CHNH₂CO₂H. Ring opening Reactions of Oxazolones. The general reaction of oxazolones with H₂O, ROH, RSH, NH₃, RNH₂ and RR'NH represented by O.CR:N.CR1R2.CO + HX → OCRHNCR1R2COX, suggested originally the thiazolidine-oxazolone formulation of penicillin. Comparison of the reactivity of V with that of IV showed the former to be rapidly hydrolyzed by 2N aqueous acid or alkali under conditions not affecting the latter. V reacts with ROH more rapidly than III. In the presence of NaOMe or PhCH₂NMe₃-OH, IVa was converted quant. to Me₂C:C(BzNH)CO₂Me, m. 130-1°. The methanolysis of 2-benzyl-4-p-methoxybenzyl-5-oxazolone in dry absolute MeOH yielded (N-phenylacetyl-p-methoxyphenylalanyl)-p-methoxyphenylalanine, m. 199-200°. The formation of the dipeptide may be due to an "ortho-ester" reaction with the imino-ether form of the oxazolone. Reaction of PhCH₂SH with III and I yielded benzyl hippurate, m. 101-2° and Me₂CHCH(NHCOCH₂Ph)COSCH₂Ph, m. 138.5°. Almost all types of oxazolones react with PhCH₂NH₂ to form α-acylaminoacyl-benzylamides. The reaction of V with d-MePhCHNH₂ in dry dioxane was followed polarimetrically and at constant rotation, produced N-benzoylphenylalanine-d-N-α-phenylethylamide, m. 178-80°, [α]_D²³ 28.5° (c 1, dioxane). The strongly enolized 2-phenyl-4-carbethoxy-5-oxazolone formed a salt with PhCH₂NH₂, converted on heating in xylene to the benzylamide, m. 132°. The reaction of

PhNH₂.HCl with III and 2-benzyl-4-sec-butyl-5-oxazolone gave the normal anilide and the corresponding acid. Reaction of V and 2-phenyl-4-isobutyl-5-oxazolone with L-HSCH₂CH-(NH₂)CO₂Me produced the normal amides, m. 128-9°, and 131-5°, resp., the NH₂ group taking precedence over the SH group in the condensation. The action of N₂H₄ on oxazolones has been clarified. The addition of 18 g.-phenyl-4-methyl-5-oxazolone to excess 60% N₂H₄.H₂O in EtOH and heating to 50-60° for 30 min. gave 17.5 g. benzoylalanine hydrazide, m. 142-4°; benzylidene derivative, m. 193-4°. Treatment of IV with N₂H₄.H₂O also gave the normal hydrazide, PhCH:C(NHBz)CONHNH₂, m. 113-14°, converted by heating the corresponding azide in xylene to 2-oxo-4-benzylidene-6-phenyl-1,3,5-oxadiazine, m. 174° (decomposition). Conversion of Me₂C:C(NHBz)CON₃ similarly produced 2-oxo-4-isopropylidene-6-phenyl-1,3,5-oxadiazine, m. 166-8°. A mixture of 5 g. IV, 10 mL. N₂H₄.H₂O and 3 mL. EtOH was refluxed for 30 min. yielding 4-benzamido-3-phenyl-5-pyrazolidone, m. 228-9°, identical with the product formed by refluxing PhCH:C(NHBz)CONHNH₂ (VIII), m. 157-8°, which N₂H₄.H₂O for 30 min. Similarly, the hydrazide Me₂C:C(NHBz)CONHNH₂, m. 192-4°, was converted into 3,3-dimethyl-4-benzoylamino-5-pyrazolidine, m. 106-8°. The hydrazide VIII was boiled in N NaOH and the sparingly soluble salt on acidification gave 6-hydroxy-5-benzyl-3-phenyl-1,2,4-triazine, m. 175-6°; Ac derivative, 187-8°. Oxidation of XIII with K₃Fe(CN)₆ produced N,N'-bis(α-benzoylamino-cinnamoyl)hydrazine, m. 265°, together with a substance, m. 186-7°, with the probable structure PhCH:C.CH(OH).NBz.C-(CHPh).CH(OH).NBz, forming PhCH₂CH(NHBz)-(CO₂H) on alkaline hydrolysis. REACTIONS OF TYPE II OXAZOLONES: Some reactions involving the double bond in type II oxazolones have been discovered. Treatment of IV in dry dioxane with 2 mol CH₂N₂ in dry Et₂O at 0° and allowing the solution to stand overnight at room temperature gave product, C₁₇H₁₃O₂N, m. 142-3°. Addition of liquid NH₃ to IVa with shaking and cooling in solid CO₂ gave a small yield of basic product, C₁₂H₁₇O₂N₃, m. 162-6°, probably by addition of 2 mol NH₃. Addition of H₂S and RSH to the double bond has been studied in connection with various syntheses of penicillamine. The addition, of 136 g. IVa in 675 mL. dry benzene to 3.38 g. Na in 675 mL. of chilled dry MeOH and 76.5 mL. PhCH₂SH produced Me₂CC(NHBz)CO₂Me, m. 137-8°, and Me₂C(SCH₂Ph)CH(NHBz)CO₂Me, m. 66-7°. The addition probably takes place after ring opening, since the oxazolone can be replaced by an acrylic ester. Similarly, IV under like conditions, gave PhCH(SCH₂Ph)CH-(NHBz)CO₂Me, m. 164°. There is no evidence of direct addition of PhCH₂SH to the double bond. Addition of H₂S to IVa and VII in the presence of Et₃N yielded Me₂C(SH)CH(NHBz)COSH and Me₂C(SH)CH(NHAc)COSH, resp. The initial step is probably the addition of H₂S to the double bond. Anhydrous MeOH saturated with H₂S at 0° treated with IVa gave 2,5,5-trimethyl-2-thiazoline-4-carboxylic acid, b₂₅ 120°; picrate, m. 159°, probably formed by addition, followed by displacement. IV similarly yielded 2-phenyl-5,5-dimethyl-2-thiazoline-4-carboxylic acid, m. 124-6°. IVa was apparently converted by treatment with alc. NaSH to 2-phenyl-4-isopropylidene-5-thiazolone, m. 100.5-101.5°. The reactivity of the Me groups in IVa is sufficient to permit condensation reactions with BzH to produce 2-phenyl-4-benzylideneisopropylidene-5-oxazolone, m. 135°. A mixture of stereoisomers, m. 134-6°, was produced by heating a mixture of 35.8 g. BzNHCH₂CO₂H, 32 g. PhCH:CHAc, 15 g. of fused NaOAc and 50 mL. Ac₂O for 3 h. at 100°. IVa is a pseudo-acid and exhibits weak violet fluorescence in Et₃N. On addition of NaOMe to IVa in MeOH, the initial intense blue-violet fluorescence in UV light due to the presence of the propenyl-oxazole soon disappears with the formation of Me₂C:C(NHBz)CO₂Me by ring opening. Miscellaneous REACTIONS OF OXAZOLONES. Excess PhMgBr was

added

to 6.0 g. 2-phenyl-4-methyl-5-oxazolone in Et₂O and after refluxing for 6 h. the reaction product was hydrolyzed and extracted with Et₂O, yielding 4.6 g. 1,1-diphenyl-2-benzoylamino-propanol, m. 192-3°. With AgClO₄ in

benzene, III in EtOH gave a complex, m. 146° (decomposition). A similar crystalline compound, m. 172° (decomposition) was formed with 2-benzyl-4-methyl-5-oxazolone (IX). Formylation of 2,4-diphenyl-5-oxazolone apparently produced a stabilized enolic form, PhC:N.CPh:COH.O, m. 110°. Oxidation of 2-phenyl-4-isobutyl- and 2-phenyl-4-benzyl-5-oxazolones with Hg(OAc)2 gave the corresponding 4,4'-bisoxazolones, m. 138-42°, and 201-202.5°, resp. PSEUDO-OXAZOLONES. According to the method of Bergmann, 12 g. PhCHBrCONHCH2CO2H was added to 5 mL. dry pyridine and 100 mL. Ac2O and after 2.5 h. at 0° was poured over ice. The solid product was dried over NaOH and crystallized from warm MeOH by cooling to -50°, yielding 64% of 2-benzylidenepseudooxazolone (2-benzylidene-3-oxazolin-5-one), m. 92-4°, hydrolyzed by 0.5N HCl in acetone to PhCH2-CONH2, m. 153-7°. An attempt to prepare 2-benzyl-4-methylene-5-oxazolone by Bergmann's method from Ph-CHClCONHCHMeCO2H gave the potent skin irritant 2-benzylidene-4-methylpseudo-5-oxazolone (X), m. 105-115°, hydrolyzed by aqueous acetone to PhCH2CONH2 and AcCO2H, suggesting that the pseudooxazolones are intermediates in the Bergmann synthesis of type II oxazolones and that, in general, the latter are in dynamic equilibrium with the pseudooxazolones. In an attempt to use pseudooxazolones for the thiazolidine-oxazolone structure suggested for penicillin, Br was added to V and the product condensed with penicillamine (XI) in the presence of AcOK and AcOH. The low order of activity noted was probably due to BrCH2COCO2H which has an activity of 6 units per mg. against Gram-pos. organisms. X (1 g.) in 40 mL. pure AcOEt was hydrogenated at several atmospheric pressure in the presence of 2 g. active Raney Ni to IX, suggesting that the thiazolidine-oxazolone structure might be accessible by reduction of the corresponding pseudooxazolone. Ice-cold pyridine (20 mL.) in 65 mL. Me2CO was mixed with 1 g. (EtO)2CHCH(NHCOCHBrPh)CO2H and after 3 h., the mixture was poured over crushed ice, extracted with CHCl3, washed with aqueous NaHCO3, dried by passage through acid-washed Al2O3, and the filtrate was evaporated, yielding 4.8 g. oily 2-benzylidene-4-(diethoxymethyl)pseudo-5-oxazolone, which failed to condense with XI. In another attempt, (EtO)2CHCH(NHCOCHClPh)CO2Me was condensed with XI to give α-Me α-chlorobenzylpenicilloate (XII). On treatment of crude XII (5.2 g.) with a mixture of 10.8 g. pyridine and 35.2 mL. Ac2O with shaking and cooling, a dark brown gum was formed, which, crystallized from Et2O at -50°, gave a "dehydropenicillin" (XIII), C16H16O4N2S, m. 90-5° (decomposition). Addnl. information in printed abstract

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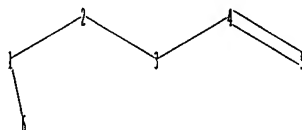
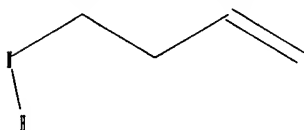
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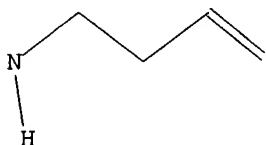
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L13 5368 L12

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L2 107785 OZON?
L3 0 L1 AND L2
L4 714963 AMINO ACID
L5 433 L2(L)L4
L6 1459162 BETA
L7 82 L5 AND L6
L8 214408 ACETIC ACID
L9 5 L7 AND L8

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L10 STRUCTURE UPLOADED
L11 47 SEARCH L10 SSS SAM
L12 13018 SEARCH L10 SSS FULL

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L13 5368 L12

=> l2 and l13

L14 109 L2 AND L13

=> l2(l)l13

L15 42 L2(L)L13

=> l8 and l15

L16 0 L8 AND L15

=> acid

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L17 4884863 ACID
(ACID OR ACIDS)

75% OF LIMIT FOR TOTAL ANSWERS REACHED

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L18 2 L15(L) L17

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L18 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

TI Improved method for synthesizing chiral or enantiomer-enriched beta-amino acids, -aldehydes, -ketones and gamma-amino alcohols

AN 2005:612232 CAPLUS

DN 143:133689

TI Improved method for synthesizing chiral or enantiomer-enriched beta-amino acids, -aldehydes, -ketones and gamma-amino alcohols

IN Walther, Jary; De Lange, Ben; Broxterman, Quirinus Bernardus; Pochlauer, Peter; Van der Sluis, Marcelles; Uiterweerd, Patrick; Falk, Heinz; Zuckerstatter, Gerhard

PA DSM Fine Chemicals Austria Nfg G.m.b.H. & Co. K.-G., Austria

SO PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005063682	A1	20050714	WO 2004-EP13354	20041125
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			AT 2003-2051	A 20031219
			AT 2004-929	A 20040528
EP 1694630	A1	20060830	EP 2004-820806	20041125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
			AT 2003-2051	A 20031219
			AT 2004-929	A 20040528
			WO 2004-EP13354	W 20041125
US 2007123589	A1	20070531	US 2006-582671	20060612
			AT 2003-2051	A 20031219
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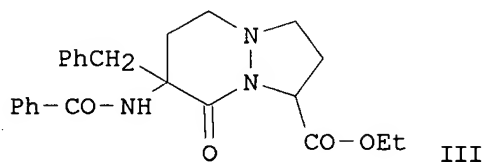
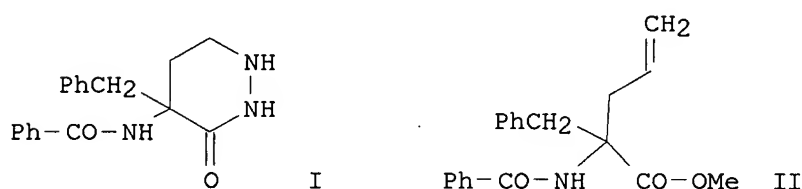
AB The title process consists of ozonolysis of allylamine derivs. in a solvent, followed by decomposition of the peroxide-containing solution by means of an oxidizing agent or reductive reprocessing into the corresponding amino compound. Thus, (R)-4-amino-4-phenyl-1-butene was converted into (R)-3-amino-3-phenyl-1-propanol by ozonolysis in methanol at -20°, followed by treatment with sodium borohydride, distillation of solvent, and workup of the product. Product was obtained in 93% yield with 99% enantio-purity; m.p. 73-74°.

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L18 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

TI A diastereoselective synthesis of the tetrahydropyridazinone core of 2-oxo-1,6-diazobicyclo[4.3.0]nonane-9-carboxylate-based peptidomimetics

starting from (S)-phenylalanine
 AN 2003:345327 CAPLUS
 DN 139:53299
 TI A diastereoselective synthesis of the tetrahydropyridazinone core of
 2-oxo-1,6-diazobicyclo[4.3.0]nonane-9-carboxylate-based peptidomimetics
 starting from (S)-phenylalanine
 AU Gardiner, James; Abell, Andrew D.
 CS Department of Chemistry, University of Canterbury, Christchurch, N. Z.
 SO Tetrahedron Letters (2003), 44(22), 4227-4230
 CODEN: TELEAY; ISSN: 0040-4039
 PB Elsevier Science Ltd.
 DT Journal
 LA English
 OS CASREACT 139:53299
 GI



AB A diastereoselective synthesis of the peptidic tetrahydropyridazinone I from (S)-phenylalanine via ozonolysis and reduction of the dialkylated amino acid II. I can be converted via 1,3-dipolar cycloaddn. to the bicyclic peptidomimetic III, an important class of β -strand mimetic serine proteases inhibitors.

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1650 GOERING H L/RAU
1597369 70/RVL
9497 3310/RPG
L19 10 GOERING H L/RAU (S) 70/RVL (S)3310/RPG

=> d l19 1-5 all

L19 ANSWER 1 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2005:995712 SCISEARCH
GA The Genuine Article (R) Number: 968MO
TI Synthesis of oxytocin analogues with replacement of sulfur by carbon gives
potent antagonists with increased stability
AU Stymiest J L; Mitchell B F; Wong S; Vederas J C (Reprint)
CS Univ Alberta, Dept Chem, Edmonton, AB T6G 2G2, Canada (Reprint); Univ
Alberta, Dept Obstet & Gynecol, Perinatal Res Ctr, Edmonton, AB TH5 3V9,
Canada
CYA Canada
SO JOURNAL OF ORGANIC CHEMISTRY, (30 SEP 2005) Vol. 70, No. 20, pp.
7799-7809.
ISSN: 0022-3263.
PB AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.

DT Article; Journal

LA English

REC Reference Count: 61

ED Entered STN: 13 Oct 2005

Last Updated on STN: 1 Dec 2005

AB The neuropeptide oxytocin 1 controls mammary and uterine smooth muscle contraction. Atosiban 2, an oxytocin antagonist, is used for prevention of preterm labor and premature birth. However, the metabolic lifetimes of such peptide drugs are short because of in vivo degradation. Facile production of oxytocin analogues with varying ring sizes wherein sulfur is replaced by carbon (methylene or methine) could be achieved by standard solid-phase peptide synthesis using olefin-bearing amino acids followed by on-resin ring-closing metathesis (RCM). These were tested for agonistic and antagonistic uteronic activity using myometrial strips taken from nonpregnant female rats. Peptide 8 showed agonistic activity in vitro ($EC_{50} = 1.4 \times 10(3) \pm 4.4 \times 10(2)$ nM) as compared to 1 ($EC_{50} = 7.0 \pm 2.1$ nM). Atosiban analogues 17 ($pA(2) = 7.8 \pm 0.1$) and 18 ($pA(2) = 8.0 \pm 0.1$) showed substantial activity compared to the parent oxytocin antagonist 2 ($pA(2) = 9.9 \pm 0.3$). Carba analogue 35 ($pA(2) = 6.1 \pm 0.1$) had an agonistic activity over 2 orders of magnitude less than its parent 3 (8.8 ± 10.5). A comparison of biological stabilities of 1,6-carba analogues of both an agonist 8 and antagonist 18 versus parent peptides 1 and 2 was conducted. The half-lives of peptides 8 and 18 in rat placental tissue were shown (Table 2) to be greatly improved versus their parents oxytocin 1 and atosiban 2, respectively. These results suggest that peptides 8 and 18 and analogues thereof may be important leads into the development of a long-lasting, commercially available therapeutic for initiation of parturition and treatment of preterm labor.

CC CHEMISTRY, ORGANIC

STP KeyWords Plus (R): RING-CLOSING METATHESIS; PRETERM LABOR; BENZOFURAN DERIVATIVES; METABOLIC STABILITY; OLEFIN METATHESIS; DICARBA ANALOGS; LACTAM ANALOGS; DOUBLE-BLIND; AMINO-ACIDS; ATOSIBAN

RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
CABROL D	2001	98	177	EUR J OBSTET GYN R B
MOUTQUIN J M	2001	108	133	BRIT J OBSTET GYNAEC
ANDERSSON K E	1983	26	56	CLIN OBSTET GYNECOL
BALDWIN J E	1992	6	1517	J CHEM RES MINIPRINT
BIAGINI S C	1998	116	2485	J CHEM SOC P1
BROUWER A J	2004	69	13662	J ORG CHEM
CALLAHAN J F	1988	53	1527	J ORG CHEM
CIRILLO R	2003	306	253	J PHARMACOL EXP THER
ENGSTROM T	1998	355	203	J PHARM
EVANS B E	1992	35	3919	J MED CHEM
GAL C S L	2004	309	414	J PHARMACOL EXP THER
GAO Y	2001	3	1617	ORG LETT
GAZAL S	2002	45	1665	J MED CHEM
GAZIS D	1978	158	663	P SOC EXP BIOL MED
GOERING H L	1948	70	3310	J AM CHEM SOC <--
GOLDENBERG R L	1998	339	313	NEW ENGL J MED
GOODWIN T M	1994	170	474	AM J OBSTET GYNECOL
GOODWIN T M	2001	11	339	J SOC GYNECOL INVEST
GRIECO P	2002	10	3731	BIOORGAN MED CHEM
GYETVAI K	1999	94	869	OBSTET GYNECOL S 2
HARGITTAI B	2000	43	4787	J MED CHEM
HARRIS J C	1998	156	35	J ENDOCRINOL
HAVASS J	2002	23	1419	PEPTIDES
HIGBY K	1999	21	35	DRUG SAFETY
JARVO E R	1999	121	11638	J AM CHEM SOC
KASMAIER U	1999	1	1763	ORG LETT
KELLER O	1974	57	1253	HELV CHIM ACTA

KUO M S	1998	8	3081	BIOORG MED CHEM LETT
MANNING M	2001	7	449	J PEPT SCI
MELIN P	1986	111	125	J ENDOCRINOL
MILLER S J	1996	118	9606	J AM CHEM SOC
MITCHELL B F	1997	57	807	BIOL REPROD
MOUTQUIN J M	2000	182	1191	AM J OBSTET GYNECOL
NELSON R	2004	104	23	AM J NURS
NICHOLSON H D	1996	1	69	REV REPROD
RAMTOHUL Y K	2002		192	THESIS U ALBERTA
REICHWEIN J F	2000		2335	EUR J ORG CHEM JUN
REICHWEIN J F	2000	65	6187	J ORG CHEM
SCHAFMEISTER C E	2000	122	5891	J AM CHEM SOC
SCHILD H O	1947	2	189	BRIT J PHARMACOL
SCHMIEDEBERG N	2002	4	59	ORG LETT
SCHOLL M	1999	1	953	ORG LETT
SCHWAB P	1996	118	100	J AM CHEM SOC
SCHWAB P	1995	34	2039	ANGEW CHEM INT EDIT
SERVITOVA L	1975	40	215	COLLECT CZECH CHEM C
SILVERSTEIN R M	1998			SPECTROMETRIC IDENTI
SMITH C W	1976	19	250	J MED CHEM
SMITH C W	1978	21	117	J MED CHEM
SPANTULESCU M D	2003	5	2963	ORG LETT
SPINELLA M J	1991	88	7443	P NATL ACAD SCI USA
STYMIEST J L	2003	5	47	ORG LETT
SWEETMAN S C	2004			MARTINDALE COMPLETE
TAUNTON J	1996	118	10412	J AM CHEM SOC
THRUIEAU C	1995	30	115	EUR J MED CHEM
TSATSARIS V	2004	64	375	DRUGS
VILLAR J	1994	16	9	RES CLIN FORUMS
WILLIAMS P D	1999	9	1311	BIOORG MED CHEM LETT
WILLIAMS R M	1998	63	2130	J ORG CHEM
WILSON L	1990	163	195	AM J OBSTET GYNECOL
WYATT P G	2002	12	1405	BIOORG MED CHEM LETT
WYATT P G	2002	12	1399	BIOORG MED CHEM LETT

L19 ANSWER 2 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 1997:518782 SCISEARCH

GA The Genuine Article (R) Number: XH601

TI Reactivity of alpha-unsaturated organozinc compounds with N-(phenylsulfanyl)iminoesters - Application to the synthesis of monosubstituted or disubstituted unsaturated alpha-aminoacids

AU Aidene M (Reprint); Barbot F; Miginiac L

CS UNIV POITIERS, ORGAN SYNTH LAB, CNRS, URA 574, F-86022 POITIERS, FRANCE

CYA FRANCE

SO JOURNAL OF ORGANOMETALLIC CHEMISTRY, (28 APR 1997) Vol. 534, No. 1-2, pp. 117-127.
ISSN: 0022-328X.

PB ELSEVIER SCIENCE SA LAUSANNE, PO BOX 564, 1001 LAUSANNE, SWITZERLAND.

DT Article; Journal

FS PHYS

LA French

REC Reference Count: 39

ED Entered STN: 1997
Last Updated on STN: 1997

AB A new general synthesis of C-substituted alpha-aminoacids is described, using at first the regioselective reaction between alpha-unsaturated organozincs and N-(phenylsulfanyl)iminoesters.

CC CHEMISTRY, INORGANIC & NUCLEAR; CHEMISTRY, ORGANIC

ST Author Keywords: N-(phenylsulfanyl)iminoesters; regioselectivity; allylic organozincs; allenic organozincs; alpha-aminoesters; alpha-aminoacide

STP KeyWords Plus (R): CHIRAL AUXILIARIES; 3-AMINO ALCOHOLS; ACID; REGIOSELECTIVITY; REAGENTS; 2-(BROMOMETHYL)ACRYLATES; IMINOESTERS;

ALKYLATION; SECONDARY; 2-AMINO

RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
ABOOD N A	1994	35	3669	TETRAHEDRON LETT
BARBOT F	1981		4016	J CHEM RES M
BARBOT F	1981		343	J CHEM RES S
BENATI L	1986	27	1739	TETRAHEDRON LETT
BHATTACHARJEE S K	1981	50	813	CURRENT SCI
BUNUEL E	1992		579	SYNLETT
CHAN L H	1967	9	231	J ORGANOMET CHEM
COURTOIS G	1989	376	235	J ORGANOMET CHEM
COURTOIS G	1993	450	33	J ORGANOMET CHEM
COURTOIS G	1993	452	5	J ORGANOMET CHEM
DAVIS F A	1977	42	398	J ORG CHEM
DEMBELE Y A	1992	3	351	TETRAHEDRON-ASYMMETR
DEMBELE Y A	1992	3	511	TETRAHEDRON-ASYMMETR
DJURIC S	1981	22	1787	TETRAHEDRON LETT
FILLMAN J	1948	70	171	J AM CHEM SOC
FRONZA G	1983	2	225	J CARBOHYD CHEM
GAUDEMAR M	1962		974	B SOC CHIM FR
GAUDEMAR M	1963		1475	B SOC CHIM FR
GENET J P	1988	44	5263	TETRAHEDRON
GENET J P	1992	33	2497	TETRAHEDRON LETT
GERSHON H	1954	76	3484	J AM CHEM SOC
GOERING H L	1948	70	3310	J AM CHEM SOC
GORDON E M	1977	99	5504	J AM CHEM SOC
GORDON E M	1980	102	1690	J AM CHEM SOC
GORDON E M	1979	44	1218	J ORG CHEM
GUO Z X	1993		874	J CHEM SOC CHEM COMM
HARPP D N	1971		4953	TETRAHEDRON LETT
HASEGAWA H	1993		489	J CHEM SOC PERK T 1
HIRAO A	1982		461	SYNTHESIS-STUTTGART
KOBAYASHI T	1979	27	2718	CHEM PHARM BULL
KOBAYASHI T	1977	99	5505	J AM CHEM SOC
LADURANTY J	1987	65	859	CAN J CHEM
LOVEY R G	1994		167	SYNLETT
MOREAU J L	1970		2171	B SOC CHIM FR
MOREAU J L	1980		363	CHEM KETENES ALLEN 1
MUKAIYAMA T	1970		3411	TETRAHEDRON LETT
PARKER E D	1961	236	3267	J BIOL CHEM
SURZUR J M	1969	269	849	CR ACAD SCI C CHIM
YANG T K	1994	59	914	J ORG CHEM

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L19 ANSWER 3 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 1995:374653 SCISEARCH
GA The Genuine Article (R) Number: RA830
TI 2 SIMILAR LACTONE-HYDROCHLORIDES WITH DIFFERENT TYPES OF HYDROGEN-BONDING
NETWORKS - CRYSTAL-STRUCTURE OF (R,S)-ALPHA-AMINO-GAMMA-CAPROLACTONE
HYDROCHLORIDE AND RACEMIC ALPHA-AMINO-GAMMA-METHYL-GAMMA-VALEROLACTONE
HYDROCHLORIDE SEMIHYDRATE
AU KAITNER B (Reprint); KIRIN S I; MESTROVIC E
CS UNIV ZAGREB, FAC SCI, DEPT CHEM, POB 153, ZVONIMIROVA 8, ZAGREB 41001,
CROATIA (Reprint); RUDJER BOSKOVIC INST, ZAGREB 41001, CROATIA
CYA CROATIA
SO JOURNAL OF CHEMICAL CRYSTALLOGRAPHY, (MAR 1995) Vol. 25, No. 3, pp.
117-122.
ISSN: 1074-1542.
PB PLENUM PUBL CORP, 233 SPRING ST, NEW YORK, NY 10013.
DT Article; Journal
FS PHYS

LA English
REC Reference Count: 24
ED Entered STN: 1995
Last Updated on STN: 1995

AB The X-ray crystal structure of (R,S)-alpha-amino-gamma-caprolactone hydrochloride (compound 1) and alpha-amino-gamma-methyl-gamma-valerolactone hydrochloride semihydrate (compound 2) are presented. Both compound 1 and compound 2 belong to the orthorhombic system. Caprolactone-hydrochloride 1 crystallizes in the space group P2(1)2(1)2(1) with a = 5.1948(7), b = 8.7404(8), c = 17.907(1) Angstrom, V = 813.0(2) Angstrom(3), Z = 4. Valerolactone-hydrochloride 2 crystallizes in the space group Pna2(1) with a = 26.771(8), b = 5.1598(7), c = 13.201(3) Angstrom, V = 1823.5(7) Angstrom(3), Z = 8. The lactone cations maintain the same, open envelope conformation in both crystals. The lactone-hydrochloride packing arrangements in 1 and 2 are distinctly different. While in 1 N-H ... Cl and N-H ... O hydrogen bonding creates two dimensional nets in the form of puckered layers perpendicular to the [001] direction, in 2 a water molecule of crystallization with an additional OW-H ... Cl hydrogen interaction assists in forming a three-dimensional hydrogen-bond network throughout the crystal.

CC CRYSTALLOGRAPHY; SPECTROSCOPY

ST Author Keywords: LACTONE-HYDROCHLORIDE; SOLID-STATE STRUCTURE; X-RAY DIFFRACTION; CONFORMATION

STP KeyWords Plus (R): NEUTRON-DIFFRACTION; SYSTEM

RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
ANON	1992			DIF4 DIFFRACTOMETER
ANON	1992			REDU4 DATA REDUCTION
ALCOCK, N W	1989	21	1835	PHYTOCHEMISTRY
ALLEN, F H	1987		S1	J CHEM SOC PERK T 2
ARMSTRONG, M D	1949	71	3399	J AM CHEM SOC
BOCELLI, G	1981	37	2106	ACTA CRYSTALLOGR SOC
BRUVO, M	1981	37	700	ACTA CRYSTALLOGR B
DELJAC, A	1993	49	1354	ACTA CRYSTALLOGR C
FILLMAN, J	1948	70	171	J AM CHEM SOC
GABE, E J	1989	22	384	J APPL CRYSTALLOGR
GOERING, H L	1948	70	3310	J AM CHEM SOC <--
IBERS, J A	1974	4	99	INT TABLES XRAY CRYST
JOHNSON, C K	1976			ORNL5138 REP
KAITNER, B	1994			UNPUB STRUCT CHEM
KIRIN, S I	1993		120	13TH M CROAT CHEM ZA
MATIJSIC, I	1988	44	159	ACTA CRYSTALLOGR
MATIJSIC, I	1989	45	1546	ACTA CRYSTALLOGR C
MO, F	1971	27	115	ACTA CRYSTALLOGR B
NARDELLI, M	1983	7	95	COMPUT CHEM
PAPAIOANNOU, D	1990	44	189	ACTA CHEM SCAND
ROGERS, D	1981	37	734	ACTA CRYSTALLOGR A
STEINER, T	1993	115	4540	J AM CHEM SOC
USHER, J J	1978	34	2012	ACTA CRYSTALLOGR B
WALKER, N	1983	39	158	ACTA CRYSTALLOGR A

L19 ANSWER 4 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 1992:670958 SCISEARCH

GA The Genuine Article (R) Number: JX822

TI SYNTHESIS OF (OPTICALLY-ACTIVE) SULFUR-CONTAINING TRIFUNCTIONAL AMINO-ACIDS BY RADICAL-ADDITION TO (OPTICALLY-ACTIVE) UNSATURATED AMINO-ACIDS

AU BROXTERMAN Q B (Reprint); KAPTEIN B; KAMPHUIS J; SCHOEMAKER H E

CS DSM RES & PATENTS, BIOORGAN CHEM SECT, POB 18, 6160 MD GELEEN, NETHERLANDS (Reprint)

CYA NETHERLANDS
 SO JOURNAL OF ORGANIC CHEMISTRY, (6 NOV 1992) Vol. 57, No. 23, pp. 6286-6294.
 ISSN: 0022-3263.
 PB AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
 DT Article; Journal
 FS PHYS; LIFE
 LA English
 REC Reference Count: 42
 ED Entered STN: 1994
 Last Updated on STN: 1994
 AB Sulfur-based radicals, generated from R-S-H-type precursors (R = alkyl, acyl) with AIBN, smoothly add to alpha-allylglycines protected at none, one, or both of the amino acid functions (NH2 and/or CO2H). Sulfur-containing trifunctional amino acids were obtained in good to excellent yields (64-100%). The solvent used for the reaction is critical. Optimal results were obtained when both the unsaturated amino acid and RSH dissolve completely in the medium (dioxane/water or methanol/water are good solvent systems). The scope of the reaction includes alpha-substituted alpha-allylglycine and derivatives as well as beta-substituted beta-allyl-beta-amino alcohols. In the case of optically active alpha-allylglycine derivatives, radical addition is accompanied by a small amount of racemization, the amount depending on the type of protection and R-S-H. The products are easily optically enriched by crystallization. Addition of sulfur-based radicals to alpha-allylglycine is believed to be an example of a general method for synthesizing optically active trifunctional amino acids from unsaturated amino acids.
 CC CHEMISTRY, ORGANIC
 STP KeyWords Plus (R): ENANTIOSELECTIVE SYNTHESIS; N-ACYLOXAZOLIDINONES; ASYMMETRIC-SYNTHESIS; DERIVATIVES; DEHYDROALANINE

RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
ADLINGTON, R M	1983		94	J CHEM OC CHEM COMMU
ALBERTSON, N F	1946	68	450	J AM CHEM SOC
BALDWIN, J E	1988		1031	J CHEM SOC CHEM COMM
BARTON, D H R	1988	44	5479	TETRAHEDRON
BECKWITH, A L J	1990		1087	J CHEM SOC CHEM COMM
BELOKON, Y N	1985		171	J CHEM SOC CHEM COMM
BOESTEN, W H J	1986	178	355	NATO ASI SER C-MATH
BOLM, C	1991	103	566	ANGEW CHEM
BURGER, K	1991	115	328	CHEM ZTG
COREY, E J	1991	56	442	J ORG CHEM
CRICH, D	1988		140	J CHEM RES SYNOP
CRICH, D	1989	45	5641	TETRAHEDRON
EASTON, C J	1991	56	5614	J ORG CHEM
ESCH, P M	1990	31	759	TETRAHEDRON LETT
EVANS, D A	1991	56	5750	J ORG CHEM
GAGE, J R	1989	68	77	ORG SYNTH
GIESE, B	1986			RADICALS ORGANIC SYN
GOERING, H L	1948	70	3310	J AM CHEM SOC <--
KAPTEIN, B				IN PRESS TETRAHEDRON
KATAGIRI, N	1991		1429	J CHEM SOC CHEM COMM
KJAER, A	1955	9	721	ACTA CHEM SCAND
KRUIZINGA, W H	1988	53	1826	J ORG CHEM
LOGUSCH, E W	1988	29	6055	TETRAHEDRON LETT
MEIJER, E M	1985		135	BIOCATALYSTS ORGANIC
MEYERS, A I	1991	56	7098	J ORG CHEM
MIYAZAWA, T	1991	6	887	CHEM EXPRESS
NEFKENS, G H L	1960	79	688	RECL TRAV CHIM PAY B
SANDLER, M	1989			DESIGN ENZYME INHIBI
SCHOLLKOPF, U	1981		969	SYNTHESIS-STUTTGART
SNIDER, B B	1991	56	4908	J ORG CHEM

SOAI, K	1991	2	781	TETRAHEDRON-ASYMMETR
SORENSEN, S P L	1902	6	137	COMPT REND TRAV LAB
TOMIOKA, K	1991	32	3095	TETRAHEDRON LETT
URBACH, H	1989	28	957	HETEROCYCLES
VRIESEMA, B K	1986	26	2045	TETRAHEDRON LETT
WALKER, M A	1991	56	5747	J ORG CHEM
WILLIAMS, R M	1991	113	9276	J AM CHEM SOC
ZEISS, H J	1990			7TH INT C PEST CHEM

STN Patent No. (RPN)	Year (RPY)	Ref. Inventor/Assignee (RIN)	Type	Ref. Patent No. (RPN)
1548032	1976	BOESTEN, W H J		1548032
DE 3817956		ZEISS, H J	APPL	GE 3817956
US 3971700	1976	BOESTEN, W H J		US 3971700
US 4172846	1979	BOESTEN, W H J		US 4172846

L19 ANSWER 5 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 1992:394911 SCISEARCH

GA The Genuine Article (R) Number: JA979

TI 2-AMINO-4-TRIMETHYLSILYL-GAMMA-BUTYROLACTONE - A SILYL ANALOGOUS HOMOTHREONINE LACTONE

AU EBELING S (Reprint); MATTHIES D; MCCARTHY D

CS UNIV HAMBURG, INST PHARMACEUT CHEM, BUNDESSTR 45, W-2000 HAMBURG 13, GERMANY

CYA GERMANY

SO JOURNAL FUR PRAKTISCHE CHEMIE-CHEMIKER-ZEITUNG, (1992) Vol. 334, No. 4, pp. 361-362.
ISSN: 0941-1216.

PB JOHANN AMBROSIOUS BARTH VERLAG, IM WEIHER 10, D-69121 HEIDELBERG, GERMANY.

DT Article; Journal

FS PHYS; ENGI

LA German

REC Reference Count: 8

ED Entered STN: 1994
Last Updated on STN: 1994

CC CHEMISTRY; CHEMISTRY, APPLIED

STP KeyWords Plus (R): AMINO-ACIDS; DERIVATIVES; LACTONIZATION

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
BENISHAI, D	1977	33	1533	TETRAHEDRON
CHENAULT, H K	1989	111	6354	J AM CHEM SOC
EBELING, S	1991	60	265	PHOSPHORUS SULFUR
GOERING, H L	1948	70	3310	J AM CHEM SOC <--
KUROKAWA, N	1986	108	6041	J AM CHEM SOC
OHFUNE, Y	1985	26	5307	TETRAHEDRON LETT
OHFUNE, Y	1986	27	6079	TETRAHEDRON LETT
WILLIAMS, R M	1988	110	1547	J AM CHEM SOC

=> d 1-10 ibib abs hit

L19 ANSWER 1 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:995712 SCISEARCH

THE GENUINE ARTICLE: 968MO

TITLE: Synthesis of oxytocin analogues with replacement of sulfur by carbon gives potent antagonists with increased stability

AUTHOR: Stymiest J L; Mitchell B F; Wong S; Vederas J C (Reprint)

CORPORATE SOURCE: Univ Alberta, Dept Chem, Edmonton, AB T6G 2G2, Canada
(Reprint); Univ Alberta, Dept Obstet & Gynecol, Perinatal
Res Ctr, Edmonton, AB TH5 3V9, Canada

COUNTRY OF AUTHOR: Canada

SOURCE: JOURNAL OF ORGANIC CHEMISTRY, (30 SEP 2005) Vol. 70, No.
20, pp. 7799-7809.
ISSN: 0022-3263.

PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036
USA.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 61

ENTRY DATE: Entered STN: 13 Oct 2005
Last Updated on STN: 1 Dec 2005

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The neuropeptide oxytocin 1 controls mammary and uterine smooth
muscle contraction. Atosiban 2, an oxytocin antagonist, is used for
prevention of preterm labor and premature birth. However, the metabolic
lifetimes of such peptide drugs are short because of in vivo degradation.
Facile production of oxytocin analogues with varying ring sizes wherein
sulfur is replaced by carbon (methylene or methine) could be achieved by
standard solid-phase peptide synthesis using olefin-bearing amino acids
followed by on-resin ring-closing metathesis (RCM). These were tested for
agonistic and antagonistic uteronic activity using myometrial strips taken
from nonpregnant female rats. Peptide 8 showed agonistic activity in
vitro ($EC_{50} = 1.4 \times 10(3) \pm 4.4 \times 10(2)$ nM) as compared to 1 ($EC_{50} = 7.0$
 ± 2.1 nM). Atosiban analogues 17 ($pA(2) = 7.8 \pm 0.1$) and 18 ($pA(2)$
 8.0 ± 0.1) showed substantial activity compared to the parent oxytocin
antagonist 2 ($pA(2) = 9.9 \pm 0.3$). Carba analogue 35 ($pA(2) = 6.1 \pm$
 0.1) had an agonistic activity over 2 orders of magnitude less than its
parent 3 (8.8 ± 10.5). A comparison of biological stabilities of
1,6-carba analogues of both an agonist 8 and antagonist 18 versus parent
peptides 1 and 2 was conducted. The half-lives of peptides 8 and 18 in
rat placental tissue were shown (Table 2) to be greatly improved versus
their parents oxytocin 1 and atosiban 2, respectively. These results
suggest that peptides 8 and 18 and analogues thereof may be important
leads into the development of a long-lasting, commercially available
therapeutic for initiation of parturition and treatment of preterm labor.

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
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GOERING H L	1948	170	13310	J AM CHEM SOC	<--
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L19 ANSWER 2 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on
STN

ACCESSION NUMBER: 1997:518782 SCISEARCH

THE GENUINE ARTICLE: XH601

TITLE: Reactivity of alpha-unsaturated organozinc compounds with
N-(phenylsulfanyl)iminoesters - Application to the
synthesis of monosubstituted or disubstituted unsaturated
alpha-aminoacids

AUTHOR: Aidene M (Reprint); Barbot F; Miginiac L

CORPORATE SOURCE: UNIV POITIERS, ORGAN SYNTH LAB, CNRS, URA 574, F-86022
POITIERS, FRANCE

COUNTRY OF AUTHOR: FRANCE

SOURCE: JOURNAL OF ORGANOMETALLIC CHEMISTRY, (28 APR 1997) Vol.
534, No. 1-2, pp. 117-127.
ISSN: 0022-328X.

PUBLISHER: ELSEVIER SCIENCE SA LAUSANNE, PO BOX 564, 1001 LAUSANNE,
SWITZERLAND.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: PHYS

LANGUAGE: French

REFERENCE COUNT: 39

ENTRY DATE: Entered STN: 1997

Last Updated on STN: 1997

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A new general synthesis of C-substituted alpha-aminoacids is described, using at first the regioselective reaction between alpha-unsaturated organozincs and N-(phenylsulfanyl)iminoesters.

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
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GOERING H L	1948	170	13310	J AM CHEM SOC	<--
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L19 ANSWER 3 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:374653 SCISEARCH

THE GENUINE ARTICLE: RA830

TITLE: 2 SIMILAR LACTONE-HYDROCHLORIDES WITH DIFFERENT TYPES OF HYDROGEN-BONDING NETWORKS - CRYSTAL-STRUCTURE OF (R,S)-ALPHA-AMINO-GAMMA-CAPROLACTONE HYDROCHLORIDE AND RACEMIC ALPHA-AMINO-GAMMA-METHYL-GAMMA-VALEROLACTONE HYDROCHLORIDE SEMIHYDRATE

AUTHOR: KAITNER B (Reprint); KIRIN S I; MESTROVIC E

CORPORATE SOURCE: UNIV ZAGREB, FAC SCI, DEPT CHEM, POB 153, ZVONIMIROVA 8, ZAGREB 41001, CROATIA (Reprint); RUDJER BOSKOVIC INST, ZAGREB 41001, CROATIA

COUNTRY OF AUTHOR: CROATIA

SOURCE: JOURNAL OF CHEMICAL CRYSTALLOGRAPHY, (MAR 1995) Vol. 25, No. 3, pp. 117-122.

ISSN: 1074-1542.

PUBLISHER: PLENUM PUBL CORP, 233 SPRING ST, NEW YORK, NY 10013.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: PHYS

LANGUAGE: English

REFERENCE COUNT: 24

ENTRY DATE: Entered STN: 1995

Last Updated on STN: 1995

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The X-ray crystal structure of (R,S)-alpha-amino-gamma-caprolactone hydrochloride (compound 1) and alpha-amino-gamma-methyl-gamma-valerolactone hydrochloride semihydrate (compound 2) are presented. Both compound 1 and compound 2 belong to the orthorhombic system. Caprolactone-hydrochloride 1 crystallizes in the space group P2(1)2(1)2(1) with a = 5.1948(7), b = 8.7404(8), c = 17.907(1) Angstrom, V = 813.0(2) Angstrom(3), Z = 4. Valerolactone-hydrochloride 2 crystallizes in the space group Pna2(1) with a = 26.771(8), b = 5.1598(7), c = 13.201(3) Angstrom, V = 1823.5(7) Angstrom(3), Z = 8. The lactone cations maintain the same, open envelope conformation in both crystals. The lactone-hydrochloride packing arrangements in 1 and 2 are distinctly different. While in 1 N-H ... Cl and N-H ... O hydrogen bonding creates two dimensional nets in the form of puckered layers perpendicular to the [001] direction, in 2 a water molecule of crystallization with an additional OW-H ... Cl hydrogen interaction assists in forming a three-dimensional hydrogen-bond network throughout the crystal.

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
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GOERING, H L	1948	170	13310	J AM CHEM SOC	<--
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L19 ANSWER 4 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1992:670958 SCISEARCH

THE GENUINE ARTICLE: JX822

TITLE: SYNTHESIS OF (OPTICALLY-ACTIVE) SULFUR-CONTAINING

TRIFUNCTIONAL AMINO-ACIDS BY RADICAL-ADDITION TO
(OPTICALLY-ACTIVE) UNSATURATED AMINO-ACIDS

AUTHOR: BROXTERMAN Q B (Reprint); KAPTEIN B; KAMPHUIS J;
SCHOEMAKER H E

CORPORATE SOURCE: DSM RES & PATENTS, BIOORGAN CHEM SECT, POB 18, 6160 MD
GELEEN, NETHERLANDS (Reprint)

COUNTRY OF AUTHOR: NETHERLANDS

SOURCE: JOURNAL OF ORGANIC CHEMISTRY, (6 NOV 1992) Vol. 57, No.
23, pp. 6286-6294.
ISSN: 0022-3263.

PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: PHYS; LIFE

LANGUAGE: English

REFERENCE COUNT: 42

ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Sulfur-based radicals, generated from R-S-H-type precursors (R =
alkyl, acyl) with AIBN, smoothly add to alpha-allylglycines protected at
none, one, or both of the amino acid functions (NH₂ and/or CO₂H).
Sulfur-containing trifunctional amino acids were obtained in good to
excellent yields (64-100%). The solvent used for the reaction is
critical. Optimal results were obtained when both the unsaturated amino
acid and RSH dissolve completely in the medium (dioxane/water or
methanol/water are good solvent systems). The scope of the reaction
includes alpha-substituted alpha-allylglycine and derivatives as well as
beta-substituted beta-allyl-beta-amino alcohols. In the case of optically
active alpha-allylglycine derivatives, radical addition is accompanied by
a small amount of racemization, the amount depending on the type of
protection and R-S-H. The products are easily optically enriched by
crystallization. Addition of sulfur-based radicals to alpha-allylglycine
is believed to be an example of a general method for synthesizing
optically active trifunctional amino acids from unsaturated amino acids.

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
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GOERING, H L	1948	170	13310	J AM CHEM SOC
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L19 ANSWER 5 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on
STN

ACCESSION NUMBER: 1992:394911 SCISEARCH

THE GENUINE ARTICLE: JA979

TITLE: 2-AMINO-4-TRIMETHYLSILYL-GAMMA-BUTYROLACTONE - A SILYL
ANALOGOUS HOMOTHREONINE LACTONE

AUTHOR: EBELING S (Reprint); MATTHIES D; MCCARTHY D

CORPORATE SOURCE: UNIV HAMBURG, INST PHARMACEUT CHEM, BUNDESSTR 45, W-2000
HAMBURG 13, GERMANY

COUNTRY OF AUTHOR: GERMANY

SOURCE: JOURNAL FUR PRAKTISCHE CHEMIE-CHEMIKER-ZEITUNG, (1992)
Vol. 334, No. 4, pp. 361-362.
ISSN: 0941-1216.

PUBLISHER: JOHANN AMBROSIOUS BARTH VERLAG, IM WEIHER 10, D-69121
HEIDELBERG, GERMANY.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: PHYS; ENGI

LANGUAGE: German

REFERENCE COUNT: 8

ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
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GOERING, H L |1948 |70 |3310 |J AM CHEM SOC <--

L19 ANSWER 6 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on
STN

ACCESSION NUMBER: 1983:197377 SCISEARCH

THE GENUINE ARTICLE: QL720

TITLE: TRITIATED PEPTIDES .13. SYNTHESIS OF [4,5-H-3-LEU2]-LOCUST
AND [3,4-H-3-PROG]-LOCUST ADIPOKINETIC HORMONE

AUTHOR: HARDY P M (Reprint); SHEPPARD P W; BRUNDISH D E; WADE R

CORPORATE SOURCE: CIBA GEIGY, RES CTR, DIV PHARMACEUT, HORSHAM RH12 4AB, W
SUSSEX, ENGLAND; UNIV EXETER, DEPT CHEM, EXETER EX4 4QD,
DEVON, ENGLAND

COUNTRY OF AUTHOR: ENGLAND

SOURCE: JOURNAL OF THE CHEMICAL SOCIETY-PERKIN TRANSACTIONS 1,
(1983) No. 4, pp. 731-734.
ISSN: 0300-922X.

PUBLISHER: ROYAL SOC CHEMISTRY, THOMAS GRAHAM HOUSE, SCIENCE PARK,
MILTON ROAD, CAMBRIDGE, CAMBS, ENGLAND CB4 4WF.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: PHYS; LIFE

LANGUAGE: English

REFERENCE COUNT: 12

ENTRY DATE: Entered STN: 1994

Last Updated on STN: 1994

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
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GOERING, H L	1948	70	3310	J AM CHEM SOC <--

L19 ANSWER 7 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on
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ACCESSION NUMBER: 1979:157628 SCISEARCH

THE GENUINE ARTICLE: GR232

TITLE: MOLECULAR-SPECIES OF SCHIFF-BASES DERIVED FROM
ORTHO-HYDROXYAROMATIC ALDEHYDES .3. SCHIFF-BASES OF
PYRIDOXAL AND ITS ANALOGS WITH UNSATURATED AMINO-ACIDS

AUTHOR: MATSUSHIMA Y (Reprint); KARUBE Y; KONO A

CORPORATE SOURCE: KYUSHU UNIV, FAC PHARMACEUT SCI, HIGASHI KU, FUKUOKA 812,
JAPAN (Reprint); KYUSHU CANC CTR RES INST, MINAMI KU,
FUKUOKA 815, JAPAN

COUNTRY OF AUTHOR: JAPAN

SOURCE: CHEMICAL & PHARMACEUTICAL BULLETIN, (1979) Vol. 27, No. 3,
pp. 703-709.
ISSN: 0009-2363.

PUBLISHER: PHARMACEUTICAL SOC JAPAN, 2-12-15-201 SHIBUYA, SHIBUYA-KU,
TOKYO 150, JAPAN.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 24

ENTRY DATE: Entered STN: 1994

Last Updated on STN: 1994

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
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GOERING, H L	1948	70	3310	J AM CHEMICAL SOC <--

L19 ANSWER 8 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on
STN

ACCESSION NUMBER: 1977:254549 SCISEARCH

THE GENUINE ARTICLE: DK728

TITLE: NEW SYNTHESIS OF AMINO-ACIDS .2. AMIDOALKYLATION OF
OLEFINS WITH GLYOXYLIC-ACID DERIVATIVES

AUTHOR: BENISHAI D (Reprint); MOSHENBERG R; ALTMAN J
 CORPORATE SOURCE: TECHNION ISRAEL INST TECHNOL, DEPT CHEM, HAIFA, ISRAEL
 COUNTRY OF AUTHOR: ISRAEL
 SOURCE: TETRAHEDRON, (1977) Vol. 33, No. 12, pp. 1533-1542.
 ISSN: 0040-4020.
 PUBLISHER: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD
 LANE, KIDLINGTON, OXFORD, ENGLAND OX5 1GB.
 DOCUMENT TYPE: Article; Journal
 LANGUAGE: English
 REFERENCE COUNT: 24
 ENTRY DATE: Entered STN: 1994
 Last Updated on STN: 1994

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
=====	=====	=====	=====	=====
GOERING, H L	1948	70	3310	J AM CHEM SOC <--

L19 ANSWER 9 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on
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ACCESSION NUMBER: 1975:385412 SCISEARCH
 THE GENUINE ARTICLE: AW947
 TITLE: NEW SYNTHESIS OF ALPHA-AMINO-ACIDS - AMIDOALKYLATION OF
 ACTIVE METHYLENE COMPOUNDS WITH GLYOXYLIC-ACID DERIVATIVES
 AUTHOR: BENISHAI D (Reprint); BERLER Z; ALTMAN J
 CORPORATE SOURCE: TECHNION ISRAEL INST TECHNOL, DEPT CHEM, HAIFA, ISRAEL
 COUNTRY OF AUTHOR: ISRAEL
 SOURCE: JOURNAL OF THE CHEMICAL SOCIETY-CHEMICAL COMMUNICATIONS,
 (1975) No. 22, pp. 905-906.
 ISSN: 0022-4936.
 PUBLISHER: ROYAL SOC CHEMISTRY, THOMAS GRAHAM HOUSE, SCIENCE PARK,
 MILTON ROAD, CAMBRIDGE, CAMBS, ENGLAND CB4 4WF.
 DOCUMENT TYPE: Article; Journal
 FILE SEGMENT: PHYS; LIFE
 LANGUAGE: English
 REFERENCE COUNT: 6
 ENTRY DATE: Entered STN: 1994
 Last Updated on STN: 1994

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
=====	=====	=====	=====	=====
GOERING H L	1948	70	3310	J AM CHEM SOC <--

L19 ANSWER 10 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on
 STN

ACCESSION NUMBER: 1974:118688 SCISEARCH
 THE GENUINE ARTICLE: S5621
 TITLE: STRUCTURAL AND CONFORMATIONAL ANALOGS OF L-METHIONINE AS
 INHIBITORS OF ENZYMATIC-SYNTHESIS OF S-ADENOSYL-L-
 METIONINE .1. SATURATED AND UNSATURATED ALIPHATIC
 AMINO-ACIDS
 AUTHOR: COULTER A W (Reprint); LOMBARDI.JB; TALALAY P
 CORPORATE SOURCE: JOHNS HOPKINS UNIV, SCH MED, DEPT PHARMACOL & EXPTL
 THERAPEUTICS, BALTIMORE, MD 21205
 COUNTRY OF AUTHOR: USA
 SOURCE: MOLECULAR PHARMACOLOGY, (1974) Vol. 10, No. 2, pp. 293-304
 ISSN: 0026-895X.
 PUBLISHER: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD
 21201-2436.
 DOCUMENT TYPE: Article; Journal
 LANGUAGE: English
 REFERENCE COUNT: 38
 ENTRY DATE: Entered STN: 1994

Last Updated on STN: 1994

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)	
GOERING H L	1948	70	3310	J AM CHEM SOC	<--

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FILE LAST UPDATED: 13 Jun 2007 (20070613/ED)

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(FILE 'HOME' ENTERED AT 07:53:25 ON 14 JUN 2007)

FILE 'CAPLUS' ENTERED AT 07:53:43 ON 14 JUN 2007

L1 43 HOMOALLYL AMINE

L2 107785 OZON?

L3 0 L1 AND L2

L4 714963 AMINO ACID

L5 433 L2(L)L4

L6 1459162 BETA

L7 82 L5 AND L6

L8 214408 ACETIC ACID

L9 5 L7 AND L8

FILE 'REGISTRY' ENTERED AT 08:08:43 ON 14 JUN 2007

L10 STRUCTURE UPLOADED

L11 47 SEARCH L10 SSS SAM

L12 13018 SEARCH L10 SSS FULL

FILE 'CAPLUS' ENTERED AT 08:09:50 ON 14 JUN 2007

L13 5368 L12

L14 109 L2 AND L13

L15 42 L2(L)L13
L16 0 L8 AND L15
L17 4884863 ACID
L18 2 L15(L)L17

FILE 'SCISEARCH' ENTERED AT 08:23:44 ON 14 JUN 2007
L19 10 S GOERING H L/RAU (S) 70/RVL (S) 3310/RPG

FILE 'CAPLUS' ENTERED AT 08:27:00 ON 14 JUN 2007

=> l19

0 GOERING H L/RAU
618058 70/RVL
4897 3310/RPG
L20 0 GOERING H L/RAU (S) 70/RVL (S) 3310/RPG

=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	9.32	358.80
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-6.24

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FILE 'CAPLUS' ENTERED AT 08:31:33 ON 14 JUN 2007
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FULL ESTIMATED COST	9.32	358.80
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-6.24

=> d his

(FILE 'HOME' ENTERED AT 07:53:25 ON 14 JUN 2007)

FILE 'CAPLUS' ENTERED AT 07:53:43 ON 14 JUN 2007
L1 43 HOMOALLYL AMINE
L2 107785 OZON?
L3 0 L1 AND L2
L4 714963 AMINO ACID
L5 433 L2(L)L4
L6 1459162 BETA
L7 82 L5 AND L6

L8 214408 ACETIC ACID
L9 5 L7 AND L8

FILE 'REGISTRY' ENTERED AT 08:08:43 ON 14 JUN 2007
L10 STRUCTURE UPLOADED
L11 47 SEARCH L10 SSS SAM
L12 13018 SEARCH L10 SSS FULL

FILE 'CAPLUS' ENTERED AT 08:09:50 ON 14 JUN 2007
L13 5368 L12
L14 109 L2 AND L13
L15 42 L2(L)L13
L16 0 L8 AND L15
L17 4884863 ACID
L18 2 L15(L)L17

FILE 'SCISEARCH' ENTERED AT 08:23:44 ON 14 JUN 2007
L19 10 S GOERING H L/RAU (S) 70/RVL (S) 3310/RPG

FILE 'CAPLUS' ENTERED AT 08:27:00 ON 14 JUN 2007
L20 0 L19

=> 12(1)18
L21 883 L2(L)L8

=> amine
279198 AMINE
258623 AMINES
L22 424834 AMINE
(AMINE OR AMINES)
95% OF LIMIT FOR TOTAL ANSWERS REACHED

=> 121(1)122
L23 9 L21(L)L22

=> d 123 1-9 ti

L23 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
TI Effects of polymer architecture and composition on the adhesion of
poly(tetrafluoroethylene)

L23 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
TI Process for producing low-molecular-weight polysaccharide and
oligosaccharide thereof

L23 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
TI Indoor air quality in museums: their existing levels, desirable conditions
and countermeasures

L23 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of ω -functional acids

L23 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
TI Aryl norbornane derivatives. I. Preparation of compounds

L23 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
TI Chemistry of cyclobutanes. I. Synthesis of methylenecyclobutanes

L23 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preliminary experiments on the synthesis of colchicine: a method for the
synthesis of ring B

L23 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

TI Molecular rearrangements in the hydronaphthalenic series

L23 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

TI β -(Hydroxyphenyl)ethylamines and their transformations. II. Synthesis of further amines and of the corresponding (hydroxyphenyl) acetic acids from natural allyl compounds

=> d l23 4 ti fbib abs

L23 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

TI Preparation of ω -functional acids

AN 1964:82493 CAPLUS

DN 60:82493

OREF 60:14392c-e

TI Preparation of ω -functional acids

IN Naudet, Maurice; Pasero, Jean; Desnuelle, Pierre

PA Institut des Corps Gras

SO 7 pp.

DT Patent

LA Unavailable

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	FR 1351737		19640207	FR 1963-926179	19630227
				FR	19630227

AB Fatty acids having a single point of unsatn. and also their derivs., such as esters, amides, alcohols, nitriles, amines, etc., were converted into ω -functional acids by ozonide formation at the double bond, followed by oxidation and chain splitting. The terminal function was first protected by acylation (reaction with acetic acid) before ozonolysis; the esterified reaction product was saponified or extracted as the alkali salt. In an example, 1 mole of oleyl acetate was dissolved in 750 cc. CHCl_3 , ozonized air bubbled through to a neg. Br test, 0.5 l. H_2O added, the pH adjusted to 9, and the mixture kept 5 hrs. at 70° while 30% H_2O_2 added portionwise and alkalinity maintained. Altogether, 250 cc. H_2O_2 and 400 cc. 30% Be NaOH were used; the solvent distilled and was recovered. At the end of the oxidation, 150 cc. 36% Be, NaOH was added, the mixture refluxed 1 hr., cooled, acidified to 10% excess by 11% Be. HCl, the organic phase. separated by decantation and washed to neutrality, pelargonic acid separated by steam distillation under reduced pressure, and the residue extracted with hot

H_2O ;

ω -hydroxy-pelargonic acid crystallized on cooling. Also prepared was ω -acetamido-pelargonic acid.

=> save temp l15 amines/a

ANSWER SET L15 HAS BEEN SAVED AS 'AMINES/A'

=> l23m and l15

2 L23M

L24 0 L23M AND L15

=> l23 and l15

L25 0 L23 AND L15

=> logoff hold

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
29.10	378.58

FULL ESTIMATED COST

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SINCE FILE	TOTAL
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CA SUBSCRIBER PRICE

ENTRY	SESSION
-0.78	-7.02

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 08:44:05 ON 14 JUN 2007

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Welcome to STN International! Enter x:x

LOGINID:SSSPTA1623PAZ

PASSWORD:

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FILE 'CAPLUS' ENTERED AT 08:46:34 ON 14 JUN 2007
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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	29.10	378.58
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-0.78	-7.02

=> help roles

CAS roles are CAS indexing terms consisting of codes that describe the new or novel information reported about a substance or a class of compounds. Specific roles have 3-letter codes. Super roles have 4-letter codes. Super roles are automatically generated from the specific roles, and are upposted for searching. Roles are available for all indexed documents from 1967 to the present.

To search a role for a specific substance, append the CAS Registry Number or a Registry File L-number answer set with a slash and the code for the role, e.g., 67-68-5/THU. To search more than one role, separate a list of roles by commas and no spaces, e.g., 67-68-5/THU,ADV. Only one role may be appended to an L-number answer set. Use the OR operator to apply multiple roles to an L-number, e.g., S L1/THU OR L1/ADV.

To search roles assigned to index headings for classes of compounds, follow the heading with a slash and the role or roles separated by commas, e.g., PHENOLS/POL,REM.

Roles are displayed in the RL (Role) field within the IT (Index Term) field. Roles are included in any display format that contains the IT or RL field. Enter SET ROLES OFF at an arrow prompt (=>) to suppress display of codes and text for roles. Enter SET ROLES CODES to display only codes. Enter SET ROLES TEXT to return to default display (codes and names). Enter HELP SET ROLES at an arrow prompt for more information.

Enter HELP THESAURUS and HELP RCODE at an arrow prompt in this file for information on using the role thesaurus to find role definitions and narrower and broader terms.

The following list contains CAS roles. Under each super role are

listed the specific roles that generate the super role.

Note that effective December 17, 2001, CAS roles were modified. The changes are summarized below and are also noted in footnotes to the list of CAS roles.

Overview of CAS role changes (effective December 17, 2001)

1. The following 4 Biological Study Roles were eliminated and replaced with more specific, newly added Biological Study roles or BSU (Biological Study, Unclassified):

BAC	Biological Activity or Effector, except Adverse
BOC	Biological Occurrence
BPR	Biological Process
MEF	Metabolic Formation

2. The following new roles were added:

COS	Cosmetic Use
DGN	Diagnostic Use
DMA	Drug Mechanism of Action
NPO	Natural Product Occurrence
PAC	Pharmacological Activity
PKT	Pharmacokinetics
BCP	Biochemical Process

RGT	Reagent
-----	---------

CPN	Combinatorial Preparation
CRT	Combinatorial Reactant
CRG	Combinatorial Reagent
CST	Combinatorial Study
CUS	Combinatorial Use

CPR	Chemical Process
EPR	Engineering Process
PYP	Physical Process

3. The following new super roles were added:

RACT	Reactant or Reagent
CMBI	Combinatorial Study

4. The name for NUU role was changed from Nonbiological Use, Unclassified to Other Use, Unclassified.

Note that effective December 13, 2006, CAS roles were modified as summarized below. The backfile will be updated in 2007.

Overview of CAS role changes (effective December 13, 2006)

1. PNU, Preparation Unclassified role is no longer being used.
2. CPR, EPR, and PYP, introduced in 2001, are no longer being used. All will be assigned the PEP, Physical, Engineering, Chemical Process.
3. DEV, Device Component Use, is no longer being used. These will be assigned to TEM, Technical or Engineering Use.

List of CAS Roles

ANST Analytical Study

ANT Analyte

AMX Analytical Matrix

ARG Analytical Reagent Use

ARU Analytical Role, Unclassified

BIOL Biological Study

ADV Adverse Effect, Including Toxicity

AGR Agricultural Use

BAC Biological Activity or Effector, Except Adverse (1)

BCP Biochemical Process (2)

BMF Bioindustrial Manufacture

BOC Biological Occurrence

BPN Biosynthetic Preparation

BPR Biological Process (1)

BSU Biological Study, Unclassified

BUU Biological Use, Unclassified

COS Cosmetic Use (2)

DGN Diagnostic Use (2)

DMA Drug Mechanism of Action (2)

FFD Food or Feed Use

MFM Metabolic Formation

NPO Natural Product Occurrence (2)

PAC Pharmacological Activity (2)

PKT Pharmacokinetics (2)

THU Therapeutic Use

CMBI Combinatorial Study (2)

CPN Combinatorial Preparation (2)

CRT Combinatorial Reactant (2)

CRG Combinatorial Reagent (2)

CST Combinatorial Study (2)

CUS Combinatorial Use (2)

FORM Formation, Nonpreparative

FMU Formation, Unclassified

GFM Geological or Astronomical Formation

MFM Metabolic Formation (1)

OCCU Occurrence

BOC Biological Occurrence (1)

GOC Geological or Astronomical Occurrence

NPO Natural Product Occurrence (2)

OCU Occurrence, Unclassified

POL Pollutant

PREP Preparation

BMF Bioindustrial Manufacture

BPN Biosynthetic Preparation

BYP Byproduct

CPN Combinatorial Preparation (2)

IMF Industrial Manufacture

PUR Purification or Recovery
 SPN Synthetic Preparation
 PROC Process
 BCP Biochemical Process (2)
 BPR Biological Process (1)
 GPR Geological or Astronomical Process
 PEP Physical, Engineering, or Chemical Process
 REM Removal or Disposal

RACT Reactant or Reagent (2,3)

RCT Reactant (3)
 CRT Combinatorial Reactant (2)
 RGT Reagent (2)
 CRG Combinatorial Reagent (2)

USES Uses

AGR Agricultural Use
 ARG Analytical Reagent Use
 BUU Biological Use, Unclassified
 CAT Catalyst Use
 COS Cosmetic Use (2)
 CUS Combinatorial Use (2)
 DGN Diagnostic Use (2)
 FFD Food or Feed Use
 MOA Modifier or Additive Use
 NUU Other Use, Unclassified (4)
 POF Polymer in Formulation
 TEM Technical or Engineered Material Use
 THU Therapeutic Use

Specific roles that are not upposted to any super roles:

MSC Miscellaneous
 PRP Properties

- (1) Used from CA Vol. 66 (1967) to Vol. 135 (2001)
- (2) Used starting with CA Vol. 136 (2002)
- (3) Searching the RCT (Reactant) role retrieves references from CA Vol. 66 (1967) to the present. Searching the RACT (Reactant or Reagent) super role retrieves references with the CRT, CRG, RGT, or RCT references starting with CA Vol. 136 (2002).
- (4) Starting with CA Vol. 136 (2002), the searchable text for the NUU role changed from NONBIOLOGICAL USE, UNCLASSIFIED/RL to OTHER USE, UNCLASSIFIED/RL. Search the code NUU/RL to retrieve records from CA Vol. 66 (1967) to the present.

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
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FULL ESTIMATED COST	30.51	379.99
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	ENTRY	SESSION
CA SUBSCRIBER PRICE	-0.78	-7.02

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FILE COVERS 1907 - 14 Jun 2007 VOL 146 ISS 25
FILE LAST UPDATED: 13 Jun 2007 (20070613/ED)

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=> d his

(FILE 'HOME' ENTERED AT 07:53:25 ON 14 JUN 2007)

FILE 'CAPLUS' ENTERED AT 07:53:43 ON 14 JUN 2007

L1 43 HOMOALLYL AMINE
L2 107785 OZON?
L3 0 L1 AND L2
L4 714963 AMINO ACID
L5 433 L2(L)L4
L6 1459162 BETA
L7 82 L5 AND L6
L8 214408 ACETIC ACID
L9 5 L7 AND L8

FILE 'REGISTRY' ENTERED AT 08:08:43 ON 14 JUN 2007

L10 STRUCTURE UPLOADED
L11 47 SEARCH L10 SSS SAM
L12 13018 SEARCH L10 SSS FULL

FILE 'CAPLUS' ENTERED AT 08:09:50 ON 14 JUN 2007

L13 5368 L12
L14 109 L2 AND L13
L15 42 L2(L)L13
L16 0 L8 AND L15
L17 4884863 ACID
L18 2 L15(L)L17

FILE 'SCISEARCH' ENTERED AT 08:23:44 ON 14 JUN 2007

L19 10 S GOERING H L/RAU (S) 70/RVL (S)3310/RPG

FILE 'CAPLUS' ENTERED AT 08:27:00 ON 14 JUN 2007

L20 0 L19
L21 883 L2(L)L8
L22 424834 AMINE
L23 9 L21(L)L22
SAVE TEMP L15 AMINES/A
L24 0 L23M AND L15
L25 0 L23 AND L15

FILE 'CAPLUS' ENTERED AT 08:48:09 ON 14 JUN 2007

=> solvent\

703417 SOLVENT

341129 SOLVENTS

SYSTEM LIMITS EXCEEDED - SEARCH ENDED

The search profile you entered was too complex or gave too many answers. Simplify or subdivide the query and try again. If you have exceeded the answer limit, enter DELETE HISTORY at an arrow prompt (=>) to remove all previous answers sets and begin at L1. Use the SAVE command to store any important profiles or answer sets before using DELETE HISTORY.

=> solvent

703417 SOLVENT

341129 SOLVENTS

SYSTEM LIMITS EXCEEDED - SEARCH ENDED

The search profile you entered was too complex or gave too many answers. Simplify or subdivide the query and try again. If you have exceeded the answer limit, enter DELETE HISTORY at an arrow prompt (=>) to remove all previous answers sets and begin at L1. Use the SAVE command to store any important profiles or answer sets before using DELETE HISTORY.

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L23 9 L21(L)L22
SAVE TEMP L15 AMINES/A
L24 0 L23M AND L15
L25 0 L23 AND L15

FILE 'CAPLUS' ENTERED AT 08:48:09 ON 14 JUN 2007

```
=> s solvent subset=l8
SUBSET IS IGNORED AS A SCOPE FOR THIS SEARCH
703417 SOLVENT
<-----User Break----->
```

```
=> s solvent
703417 SOLVENT
341129 SOLVENTS
SYSTEM LIMITS EXCEEDED - SEARCH ENDED
The search profile you entered was too complex or gave too many
answers. Simplify or subdivide the query and try again. If you have
exceeded the answer limit, enter DELETE HISTORY at an arrow prompt
(=>) to remove all previous answers sets and begin at L1. Use the
SAVE command to store any important profiles or answer sets before
using DELETE HISTORY.
```

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=> d his
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(FILE 'HOME' ENTERED AT 07:53:25 ON 14 JUN 2007)

FILE 'CAPLUS' ENTERED AT 07:53:43 ON 14 JUN 2007

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L1      43 HOMOALLYL AMINE
L2      107785 OZON?
L3      0 L1 AND L2
L4      714963 AMINO ACID
L5      433 L2(L)L4
L6      1459162 BETA
L7      82 L5 AND L6
L8      214408 ACETIC ACID
L9      5 L7 AND L8
```

FILE 'REGISTRY' ENTERED AT 08:08:43 ON 14 JUN 2007

```
L10     STRUCTURE UPLOADED
L11     47 SEARCH L10 SSS SAM
L12     13018 SEARCH L10 SSS FULL
```

FILE 'CAPLUS' ENTERED AT 08:09:50 ON 14 JUN 2007

```
L13     5368 L12
L14     109 L2 AND L13
L15     42 L2(L)L13
L16     0 L8 AND L15
L17     4884863 ACID
L18     2 L15(L)L17
```

FILE 'SCISEARCH' ENTERED AT 08:23:44 ON 14 JUN 2007

```
L19     10 S GOERING H L/RAU (S) 70/RVL (S)3310/RPG
```

FILE 'CAPLUS' ENTERED AT 08:27:00 ON 14 JUN 2007

```
L20     0 L19
L21     883 L2(L)L8
L22     424834 AMINE
L23     9 L21(L)L22
        SAVE TEMP L15 AMINES/A
L24     0 L23M AND L15
L25     0 L23 AND L15
```

FILE 'CAPLUS' ENTERED AT 08:48:09 ON 14 JUN 2007

```
=> allylamine or (allyl amine)
7851 ALLYLAMINE
675 ALLYLAMINES
```


8124 ALLYLAMINE
 (ALLYLAMINE OR ALLYLAMINES)
 106509 ALLYL
 132 ALLYLS
 106554 ALLYL
 (ALLYL OR ALLYLS)
 279198 AMINE
 258623 AMINES
 424834 AMINE
 (AMINE OR AMINES)
 618 ALLYL AMINE
 (ALLYL(W)AMINE)
 L26 8582 ALLYLAMINE OR (ALLYL AMINE)

=> l21 and l26
 L27 2 L21 AND L26

=> d l27 1-2 ti

L27 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Effects of polymer architecture and composition on the adhesion of
 poly(tetrafluoroethylene)

L27 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Acylated Allylamines

=> d l27 s ti fbib abs
 's' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS ----- GI and AB
 ALL ----- BIB, AB, IND, RE
 APPS ----- AI, PRAI
 BIB ----- AN, plus Bibliographic Data and PI table (default)
 CAN ----- List of CA abstract numbers without answer numbers
 CBIB ----- AN, plus Compressed Bibliographic Data
 CLASS ----- IPC, NCL, ECLA, FTERM
 DALL ----- ALL, delimited (end of each field identified)
 DMAX ----- MAX, delimited for post-processing
 FAM ----- AN, PI and PRAI in table, plus Patent Family data
 FBIB ----- AN, BIB, plus Patent FAM
 IND ----- Indexing data
 IPC ----- International Patent Classifications
 MAX ----- ALL, plus Patent FAM, RE
 PATS ----- PI, SO
 SAM ----- CC, SX, TI, ST, IT
 SCAN ----- CC, SX, TI, ST, IT (random display, no answer numbers;
 SCAN must be entered on the same line as the DISPLAY,
 e.g., D SCAN or DISPLAY SCAN)
 STD ----- BIB, CLASS

 IABS ----- ABS, indented with text labels
 IALL ----- ALL, indented with text labels
 IBIB ----- BIB, indented with text labels
 IMAX ----- MAX, indented with text labels
 ISTD ----- STD, indented with text labels

 OBIB ----- AN, plus Bibliographic Data (original)
 OIBIB ----- OBIB, indented with text labels

 SBIB ----- BIB, no citations

SIBIB ----- IBIB, no citations

HIT ----- Fields containing hit terms

HITIND ----- IC, ICA, ICI, NCL, CC and index field (ST and IT) containing hit terms

HITRN ----- HIT RN and its text modification

HITSTR ----- HIT RN, its text modification, its CA index name, and its structure diagram

HITSEQ ----- HIT RN, its text modification, its CA index name, its structure diagram, plus NTE and SEQ fields

FHITSTR ----- First HIT RN, its text modification, its CA index name, and its structure diagram

FHITSEQ ----- First HIT RN, its text modification, its CA index name, its structure diagram, plus NTE and SEQ fields

KWIC ----- Hit term plus 20 words on either side

OCC ----- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of formats include: TI; TI,AU; BIB,ST; TI,IND; TI,SO. You may specify the format fields in any order and the information will be displayed in the same order as the format specification.

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ENTER DISPLAY FORMAT (BIB):end

=> d 127 ti fbib abs

L27 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

TI Effects of polymer architecture and composition on the adhesion of poly(tetrafluoroethylene)

AN 2006:623782 CAPLUS

DN 146:296544

TI Effects of polymer architecture and composition on the adhesion of poly(tetrafluoroethylene)

AU Tu, Chen-Yuan; Liu, Ying-Ling; Luo, Min-Tzu; Lee, Kueir-Rarn; Lai, Juin-Yih

CS Department of Chemical Engineering, Chung Yuan University, Taoyuan, 32023, Taiwan

SO ChemPhysChem (2006), 7(6), 1355-1360

CODEN: CPCHFT; ISSN: 1439-4235

PB Wiley-VCH Verlag GmbH & Co. KGaA

DT Journal

LA English

AB Poly(glycidyl methacrylate), PGMA, chains in linear and arborescent structures were incorporated onto surfaces of poly(tetrafluoroethylene), PTFE, films by hydrogen plasma and ozone treatment and atom transfer radical polymerization. The epoxide groups of the PGMA chains were further reacted with acetic acid (AAc), oxalic acid (XAc), allyl amine (AA), and ethylenediamine (EDN) to introduce hydroxyl and amine groups to the surfaces of the PTFE films. Surface characterizations performed by Fourier Transform IR attenuated total reflectance (FTIR-ATR) spectroscopy and XPS confirmed the surface modification and the chemical structure. The PGMA chains in arborescent structures show a high effectiveness for the enhancement of the adhesion of PTFE films. The adhesion of PTFE films was also significantly enhanced by ring-opening reactions of the PGMA epoxide groups with acetic acid and amine compds. A high value of 9.5 N cm⁻¹ in the optimum 180° peel strength test was observed with PTFE/copper assemblies.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> logoff hold\
'HOLD\' IS NOT VALID HERE
For an explanation, enter "HELP LOGOFF".

=> logoff hold		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	14.24	394.23
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-0.78	-7.80

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STN INTERNATIONAL SESSION SUSPENDED AT 08:53:57 ON 14 JUN 2007